



Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

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Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 1 of 5) (Last updated May 7, 2013; last reviewed May 7, 2013)

Opportunistic Infections	Indication	Preferred	Alternative
<i>Pneumocystis pneumonia (PCP)</i>	<ul style="list-style-type: none"> • CD4 count <200 cells/μL (AI), <i>or</i> • Oropharyngeal candidiasis (AII), <i>or</i> • CD4 <14% (BII), <i>or</i> • History of AIDS-defining illness (BII), <i>or</i> • CD4 count >200 but <250 cells/μL if monitoring CD4 cell count every 3 months is not possible (BII) <p>Note: Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).</p>	<ul style="list-style-type: none"> • TMP-SMX^a 1 double-strength (DS) PO daily (AI), <i>or</i> • TMP-SMX^a 1 single-strength (SS) daily (AI) 	<ul style="list-style-type: none"> • TMP-SMX^a 1 DS PO TIW (BI), <i>or</i> • Dapsone^b 100 mg PO daily or 50 mg PO BID (BI), <i>or</i> • Dapsone^b 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly (BI), <i>or</i> • (Dapsone^b 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (BI); <i>or</i> • Aerosolized pentamidine 300 mg via Respigard II™ nebulizer every month (BI), <i>or</i> • Atovaquone 1500 mg PO daily (BI), <i>or</i> • (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily (CIII)
<i>Toxoplasma gondii encephalitis</i>	<ul style="list-style-type: none"> • Toxoplasma IgG-positive patients with CD4 count <100 cells/μL (AII); • Seronegative patients receiving PCP prophylaxis not active against toxoplasmosis should have toxoplasma serology retested if CD4 count decline to <100 cells/μL (CIII). Prophylaxis should be initiated if seroconversion occurred (AII). <p>Note: All regimens recommended for primary prophylaxis against toxoplasmosis are also effective as PCP prophylaxis.</p>	<ul style="list-style-type: none"> • TMP-SMX^a 1 DS PO daily (AII) 	<ul style="list-style-type: none"> • TMP-SMX^a 1 DS PO TIW (BIII), <i>or</i> • TMP-SMX^a 1 SS PO daily (BIII), <i>or</i> • Dapsone^b 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly (BI), <i>or</i> • (Dapsone^b 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (BI); <i>or</i> • Atovaquone 1500 mg PO daily (CIII); <i>or</i> • (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily (CIII)
<i>Mycobacterium tuberculosis infection (TB)</i> (i.e., treatment of latent TB infection [LTBI])	<ul style="list-style-type: none"> • (+) screening test for LTBI^c, with no evidence of active TB, and no prior treatment for active TB or LTBI (AI), <i>or</i> • Close contact with a person with infectious TB, with no evidence of active TB, regardless of screening test results (AII). 	<ul style="list-style-type: none"> • (INH 300 mg + pyridoxine 25 mg) PO daily x 9 months (AII), <i>or</i> • INH 900 mg PO BIW (by DOT) + pyridoxine 25 mg PO daily x 9 months (BII). 	<ul style="list-style-type: none"> • Rifampin 600 mg PO daily x 4 months (BIII), <i>or</i> • Rifabutin (dose adjusted based on concomitant ART)^d x 4 months (BIII). <p>For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or public health authorities (AII).</p>
Disseminated <i>Mycobacterium avium</i> complex (MAC) disease	<p>CD4 count <50 cells/μL—after ruling out active disseminated MAC disease based on clinical assessment (AI).</p>	<ul style="list-style-type: none"> • Azithromycin 1200 mg PO once weekly (AI), <i>or</i> • Clarithromycin 500 mg PO BID (AI), <i>or</i> • Azithromycin 600 mg PO twice weekly (BIII) 	<p>Rifabutin (dose adjusted based on concomitant ART)^d (BI); rule out active TB before starting rifabutin</p>

Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 2 of 5)

Opportunistic Infections	Indication	Preferred	Alternative
<i>Streptococcus pneumoniae</i> infection	For individuals who have not received any pneumococcal vaccine, regardless of CD4 count, followed by: <ul style="list-style-type: none"> • if CD4 count ≥ 200 cells/μL • if CD4 count < 200 cells/μL 	PCV13 0.5 mL IM x 1 (AI) . PPV23 0.5 mL IM at least 8 weeks after the PCV13 vaccine (AII) . PPV23 can be offered at least 8 weeks after receiving PCV13 (CIII) or can wait until CD4 count increased to > 200 cells/ μ L (BIII) .	PPV23 0.5 mL IM x 1 (BII)
	For individuals who have previously received PPV23	One dose of PCV13 should be given at least 1 year after the last receipt of PPV23 (AII) .	
	<u>Re-vaccination</u> <ul style="list-style-type: none"> • If age 19–64 years and ≥ 5 years since the first PPV23 dose • If age ≥ 65 years, and if ≥ 5 years since the previous PPV23 dose 	<ul style="list-style-type: none"> • PPV23 0.5 mL IM x 1 (BIII) • PPV23 0.5 mL IM x 1 (BIII) 	
Influenza A and B virus infection	All HIV-infected patients (AIII)	Inactivated influenza vaccine annually (per recommendation for the season) (AIII) Live-attenuated influenza vaccine is contraindicated in HIV-infected patients (AIII) .	
Syphilis	<ul style="list-style-type: none"> • For individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within past 90 days (AII), <i>or</i> • For individuals exposed to a sex partner > 90 days before syphilis diagnosis in the partner, if serologic test results are not available immediately and the opportunity for follow-up is uncertain (AIII) 	Benzathine penicillin G 2.4 million units IM for 1 dose (AII)	<i>For penicillin-allergic patients:</i> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 14 days (BII), <i>or</i> • Ceftriaxone 1 g IM or IV daily for 8–10 days (BII), <i>or</i> • Azithromycin 2 g PO for 1 dose (BII) – not recommended for MSM or pregnant women (AII)
<i>Histoplasma capsulatum</i> infection	CD4 count ≤ 150 cells/ μ L and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (> 10 cases/100 patient-years) (BI)	Itraconazole 200 mg PO daily (BI)	

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Opportunistic Infections	Indication	Preferred	Alternative
Coccidioidomycosis	A new positive IgM or IgG serologic test in patients who live in a disease-endemic area and with CD4 count <250 cells/ μ L (BIII)	Fluconazole 400 mg PO daily (BIII)	
Varicella-zoster virus (VZV) infection	<p><u>Pre-exposure prevention:</u> Patients with CD4 counts \geq200 cells/μL who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV (CIII)</p> <p>Note: Routine VZV serologic testing in HIV-infected adults and adolescents is not recommended.</p> <p><u>Post-exposure prevention: (AIII)</u> Close contact with a person with chickenpox or herpes zoster; and is susceptible (i.e., no history of vaccination or of either condition, or known to be VZV seronegative)</p>	<p><u>Pre-exposure prevention:</u> Primary varicella vaccination (Varivax™), 2 doses (0.5 mL SQ each) administered 3 months apart (CIII).</p> <p>If vaccination results in disease because of vaccine virus, treatment with acyclovir is recommended (AIII).</p> <p><u>Post-exposure prevention:</u> Varicella-zoster immune globulin (VariZIG™) 125 international units per 10 kg (maximum 625 international units) IM, administered as soon as possible and within 10 days after exposure (AIII)</p> <p>Note: VariZIG can be obtained only under a treatment IND (800-843-7477, FFF Enterprises).</p> <p>Individuals receiving monthly high-dose IVIG (>400 mg/kg) are likely to be protected if the last dose of IVIG was administered <3 weeks before exposure.</p>	<p><u>Pre-exposure prevention:</u> VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts (BIII).</p> <p><u>Alternative post-exposure prevention:</u></p> <ul style="list-style-type: none"> • Acyclovir 800 mg PO 5 x/day for 5–7 days (BIII), <i>or</i> • Valacyclovir 1 g PO TID for 5–7 days (BIII) <p>These alternatives have not been studied in the HIV population.</p> <p>If antiviral therapy is used, varicella vaccines should not be given until at least 72 hours after the last dose of the antiviral drug.</p>
Human Papillomavirus (HPV) infection	Females aged 13–26 years (BIII)	<ul style="list-style-type: none"> • HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII), <i>or</i> • HPV bivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII) 	
	Males aged 13–26 years (BIII)	HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII)	

Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 4 of 5)

Opportunistic Infections	Indication	Preferred	Alternative
Hepatitis A virus (HAV) infection	HAV-susceptible patients with chronic liver disease, or who are injection-drug users, or MSM (AII) .	Hepatitis A vaccine 1 mL IM x 2 doses at 0 and 6–12 months (AII) . IgG antibody response should be assessed 1 month after vaccination; non-responders should be revaccinated when CD4 count >200 cells/μL. (BIII) .	<u>For patients susceptible to both HAV and hepatitis B virus (HBV) infection (see below):</u> Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) (AII)
Hepatitis B virus (HBV) infection	<ul style="list-style-type: none"> • Patients without chronic HBV or without immunity to HBV (i.e., anti-HBs <10 international units/mL) (AII) • Patients with isolated anti-HBc and negative HBV DNA (BII) • Early vaccination is recommended before CD4 count falls below 350 cells/μL (AII). However, in patients with low CD4 cell counts, vaccination should not be deferred until CD4 count reaches >350 cells/μL, because some patients with CD4 counts <200 cells/μL do respond to vaccination (AII). • In general, patients should be vaccinated, regardless of CD4 cell counts (CIII). 	<ul style="list-style-type: none"> • HBV vaccine IM (Engerix-B 20 μg/mL or Recombivax HB 10 μg/mL), 0, 1, and 6 months (AII), <i>or</i> • Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) (AII) <p>Anti-HBs should be obtained 1 month after completion of the vaccine series. Patients with anti-HBs <10 international units/mL at 1 month are considered non-responders. (BIII).</p>	Some experts recommend vaccinating with 40-μg doses of either HBV vaccine (CIII) .
	<p><u>Vaccine Non-Responders:</u></p> <ul style="list-style-type: none"> • Anti-HBs <10 international units/mL 1 month after vaccination series • For patients with low CD4 counts at time of first vaccine series, some specialists might delay re-vaccination until after sustained increase in CD4 count with ART (CIII). 	Re-vaccinate with a second vaccine series (BIII)	Some experts recommend re-vaccinating with 40 μg doses of either HBV vaccine (CIII) .
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients. Recommendations are based on region of travel, malaria risks, and drug susceptibility in the region. Refer to the following website for the most recent recommendations based on region and drug susceptibility: http://www.cdc.gov/malaria/ .	

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Opportunistic Infections	Indication	Preferred	Alternative
Penicilliosis	Patients with CD4 cell counts <100 cells/ μ L who live or stay for a long period in rural areas in northern Thailand, Vietnam, or Southern China (BI)	Itraconazole 200 mg once daily (BI)	Fluconazole 400 mg PO once weekly (BI)

Key to Acronyms: anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody; ART = antiretroviral therapy; BID = twice daily; BIW = twice a week; CD4 = CD4 T lymphocyte cell; DOT = directly observed therapy; DS = double strength; HAV = hepatitis A virus; HBV = hepatitis B virus; HPV = human papillomavirus; IgG = immunoglobulin G; IgM = immunoglobulin M; IM = intramuscular; INH = isoniazid; IV = intravenously; IVIG = intravenous immunoglobulin; LTBI = latent tuberculosis infection; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis pneumonia*; PCV13 = 13-valent pneumococcal conjugate vaccine; PO = orally; PPV23 = 23-valent pneumococcal polysaccharides vaccine; SQ = subcutaneous; SS = single strength; TB = tuberculosis; TIW = thrice weekly; TMP-SMX = Trimethoprim-sulfamethoxazole; VZV = varicella zoster virus

^a TMP-SMX DS once daily also confers protection against toxoplasmosis and many respiratory bacterial infections; lower dose also likely confers protection

^b Patients should be tested for glucose-6-phosphate dehydrogenase (G6PD) before administration of dapsone or primaquine. Alternative agent should be used in patients found to have G6PD deficiency

^c Screening tests for LTBI include tuberculin skin test (TST) or interferon-gamma release assays (IGRA)

^d Refer to [Table 5](#) for dosing recommendation

Evidence Rating:

Strength of Recommendation:

A: Strong recommendation for the statement

B: Moderate recommendation for the statement

C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints

II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes

III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 1 of 23) (Last updated July 8, 2013; last reviewed July 8, 2013)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Pneumocystis</i> Pneumonia (PCP)	<p>Patients who develop PCP despite TMP-SMX prophylaxis can usually be treated with standard doses of TMP-SMX (BIII).</p> <p>Duration of PCP treatment: 21 days (AII)</p> <p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> • TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day IV given q6h or q8h (AI), may switch to PO after clinical improvement (AI) <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> • TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day, given PO in 3 divided doses (AI), or • TMP-SMX: (160 mg/800 mg or DS) 2 tablets PO TID (AI) <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> • TMP-SMX DS: 1 tablet PO daily (AI), or • TMP-SMX (80 mg/400 mg or SS): 1 tablet PO daily (AI) 	<p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> • Pentamidine 4 mg/kg IV daily infused over ≥60 minutes (AI); can reduce dose to 3 mg/kg IV daily because of toxicities (BI), or • Primaquine 30 mg (base) PO daily + (clindamycin 600 mg q6h IV or 900 mg IV q8h) or (clindamycin 300 mg PO q6h or 450 mg PO q8h) (AI) <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> • Dapsone 100 mg PO daily + TMP 5 mg/kg PO TID (BI), or • Primaquine 30 mg (base) PO daily + (clindamycin 300 mg PO q6h or 450 mg PO q8h) (BI), or • Atovaquone 750 mg PO BID with food (BI) <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> • TMP-SMX DS: 1 tablet PO TIW (BI), or • Dapsone 100 mg PO daily (BI), or • Dapsone 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly (BI), or • (Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (BI), or • Aerosolized pentamidine 300 mg monthly via Respigard II™ nebulizer (BI), or • Atovaquone 1500 mg PO daily (BI), or • (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily (CIII) 	<p><u>Indications for Adjunctive Corticosteroids (AI):</u></p> <ul style="list-style-type: none"> • PaO₂ <70 mmHg at room air, or • Alveolar-arterial O₂ gradient >35 mmHg <p><u>Prednisone Doses (Beginning as Early as Possible and Within 72 Hours of PCP Therapy) (AI):</u></p> <ul style="list-style-type: none"> • Days 1–5: 40 mg PO BID • Days 6–10: 40 mg PO daily • Days 11–21: 20 mg PO daily <p>IV methylprednisolone can be administered as 75% of prednisone dose.</p> <p>Benefit of corticosteroid if started after 72 hours of treatment is unknown, but some clinicians will use it for moderate-to-severe PCP (BIII).</p> <p>Whenever possible, patients should be tested for G6PD before use of dapsone or primaquine. Alternative therapy should be used in patients found to have G6PD deficiency.</p> <p>Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).</p> <p>If TMP-SMX is discontinued because of a mild adverse reaction, re-institution should be considered after the reaction resolves (AII). The dose can be increased gradually (desensitization) (BI), reduced, or the frequency modified (CIII).</p> <p>TMP-SMX should be permanently discontinued in patients with possible or definite Stevens-Johnson Syndrome or toxic epidermal necrosis (AII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 2 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Toxoplasma gondii</i> Encephalitis	<p><u>Treatment of Acute Infection (AI):</u></p> <ul style="list-style-type: none"> Pyrimethamine 200 mg PO 1 time, followed by weight-based therapy: <ul style="list-style-type: none"> If <60 kg, pyrimethamine 50 mg PO once daily + sulfadiazine 1000 mg PO q6h + leucovorin 10–25 mg PO once daily If ≥60 kg, pyrimethamine 75 mg PO once daily + sulfadiazine 1500 mg PO q6h + leucovorin 10–25 mg PO once daily Leucovorin dose can be increased to 50 mg daily or BID. <p><u>Duration for Acute Therapy:</u></p> <ul style="list-style-type: none"> At least 6 weeks (BII); longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> Pyrimethamine 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) + leucovorin 10–25 mg PO daily (AI) 	<p><u>Treatment of Acute Infection:</u></p> <ul style="list-style-type: none"> Pyrimethamine (leucovorin)* + clindamycin 600 mg IV or PO q6h (AI), or TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) IV or PO BID (BI), or Atovaquone 1500 mg PO BID with food + pyrimethamine (leucovorin)* (BII), or Atovaquone 1500 mg PO BID with food + sulfadiazine 1000–1500 mg PO q6h (weight-based dosing, as in preferred therapy) (BII), or Atovaquone 1500 mg PO BID with food (BII), or Pyrimethamine (leucovorin)* + azithromycin 900–1200 mg PO daily (CII) <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> Clindamycin 600 mg PO q8h + (pyrimethamine 25–50 mg + leucovorin 10–25 mg) PO daily (BI), or TMP-SMX DS 1 tablet BID (BII), or Atovaquone 750–1500 mg PO BID + (pyrimethamine 25 mg + leucovorin 10 mg) PO daily (BII), or Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses (BII)), or Atovaquone 750–1500 mg PO BID with food (BII) <p>* Pyrimethamine and leucovorin doses are the same as for preferred therapy.</p>	<p>Adjunctive corticosteroids (e.g., dexamethasone) should only be administered when clinically indicated to treat mass effect associated with focal lesions or associated edema (BIII); discontinue as soon as clinically feasible.</p> <p>Anticonvulsants should be administered to patients with a history of seizures (AIII) and continued through acute treatment, but should not be used as seizure prophylaxis (AIII).</p> <p>If clindamycin is used in place of sulfadiazine, additional therapy must be added to prevent PCP (AII).</p>
Cryptosporidiosis	<ul style="list-style-type: none"> Initiate or optimize ART for immune restoration to CD4 count >100 cells/μL (AII), and Aggressive oral or IV rehydration and replacement of electrolyte loss (AIII), and Symptomatic treatment of diarrhea with anti-motility agents (AIII). 	<p>No therapy has been shown to be effective without ART. Trial of these agents may be used in conjunction with, but not instead of, ART:</p> <ul style="list-style-type: none"> Nitazoxanide 500–1000 mg PO BID for 14 days (CIII), or Paromomycin 500 mg PO QID for 14–21 days (CIII) <p>• With optimized ART, symptomatic treatment and rehydration and electrolyte replacement</p>	<p>Tincture of opium may be more effective than loperamide in management of diarrhea (CIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 3 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Microsporidiosis	<p><u>For GI Infections Caused by <i>Enterocytozoon bienuesi</i>:</u></p> <ul style="list-style-type: none"> • Initiate or optimize ART as immune restoration to CD4 count >100 cells/μL (AII); <i>plus</i> • Manage severe dehydration, malnutrition, and wasting by fluid support (AII) and nutritional supplement (AIII) <p><u>For Intestinal and Disseminated (Not Ocular) Infections Caused by Microsporidia Other Than <i>E. bienuesi</i> and <i>Vittaforma corneae</i>:</u></p> <ul style="list-style-type: none"> • Albendazole 400 mg PO BID (AII), continue until CD4 count >200 cells/μL for >6 months after initiation of ART (BIII) <p><u>For Ocular Infection:</u></p> <ul style="list-style-type: none"> • Topical fumagillin bicyclohexylammonium (Fumidil B) eye drops: 3 mg/mL in saline (fumagillin 70 μg/mL)—2 drops q2h for 4 days, then 2 drops QID (investigational use only in United States) (BII) + albendazole 400 mg PO BID, for management of systemic infection (BIII) • Therapy should be continued until resolution of ocular symptoms and CD4 count increase to >200 cells/μL for >6 months in response to ART (CIII). 	<p><u>For GI Infections Caused by <i>E. bienuesi</i>:</u></p> <ul style="list-style-type: none"> • Fumagillin 60 mg/day (BII) and TNP-470 (a synthetic analog of fumagillin) (BIII) may be effective, but neither is available in the United States. • Nitazoxanide (1000 mg BID) may have some effect but response may be minimal in patients with low CD4 cell counts (CIII). <p><u>For Disseminated Disease Attributed to <i>Trachipleistophora</i> or <i>Anncaliia</i>:</u></p> <ul style="list-style-type: none"> • Itraconazole 400 mg PO daily + albendazole 400 mg PO BID (CIII) 	<p>Anti-motility agents can be used for diarrhea control if required (BIII).</p>

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Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Mycobacterium tuberculosis</i> (TB) Disease	<p>After collecting specimen for culture and molecular diagnostic tests, empiric TB treatment should be started in individuals with clinical and radiographic presentation suggestive of TB (AIII).</p> <p>Refer to Table 3 for dosing recommendations.</p> <p><u>Initial Phase (2 Months, Given Daily, 5–7 Times/Week by DOT) (AI):</u></p> <ul style="list-style-type: none"> • INH + [RIF or RFB] + PZA + EMB (AI), <p><u>Continuation Phase:</u></p> <ul style="list-style-type: none"> • INH + (RIF or RFB) daily (5–7 times/week) or TIW (AIII) <p><u>Total Duration of Therapy (For Drug-Susceptible TB):</u></p> <ul style="list-style-type: none"> • Pulmonary TB: 6 months (BII) • Pulmonary TB and culture-positive after 2 months of TB treatment: 9 months (BII) • Extra-pulmonary TB w/CNS infection: 9–12 months (BII); • Extra-pulmonary TB w/bone or joint involvement: 6 to 9 months (BII); • Extra-pulmonary TB in other sites: 6 months (BII) <p>Total duration of therapy should be based on number of doses received, not on calendar time</p>	<p>Treatment for Drug-Resistant TB</p> <p><u>Resistant to INH:</u></p> <ul style="list-style-type: none"> • (RIF or RFB) + EMB + PZA + (moxifloxacin or levofloxacin) for 2 months (BII); followed by (RIF or RFB) + EMB + (moxifloxacin or levofloxacin) for 7 months (BII) <p><u>Resistant to Rifamycins +/- Other Drugs:</u></p> <ul style="list-style-type: none"> • Regimen and duration of treatment should be individualized based on resistance pattern, clinical and microbiological responses, and in close consultation with experienced specialists (AIII). 	<p>Adjunctive corticosteroid improves survival for TB meningitis and pericarditis (AI). See text for drug, dose, and duration recommendations.</p> <p>RIF is not recommended for patients receiving HIV PI because of its induction of PI metabolism (AII).</p> <p>RFB is a less potent CYP3A4 inducer than RIF and is preferred in patients receiving PIs.</p> <p>Once weekly rifapentine can result in development of rifamycin resistance in HIV-infected patients and is not recommended (AI).</p> <p>Therapeutic drug monitoring should be considered in patients receiving rifamycin and interacting ART.</p> <p>Paradoxical IRIS that is not severe can be treated with NSAIDs without a change in TB or HIV therapy (BIII).</p> <p>For severe IRIS reaction, consider prednisone and taper over 4 weeks based on clinical symptoms (BIII).</p> <p>For example:</p> <ul style="list-style-type: none"> • <u>If receiving RIF</u>: prednisone 1.5 mg/kg/day for 2 weeks, then 0.75 mg/kg/day for 2 weeks • <u>If receiving RFB</u>: prednisone 1.0 mg/kg/day for 2 weeks, then 0.5 mg/kg/day for 2 weeks <p>A more gradual tapering schedule over a few months may be necessary for some patients.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 5 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Disseminated <i>Mycobacterium avium</i> Complex (MAC) Disease	<p><u>At Least 2 Drugs as Initial Therapy With:</u></p> <ul style="list-style-type: none"> • Clarithromycin 500 mg PO BID (AI) + ethambutol 15 mg/kg PO daily (AI), <i>or</i> • (Azithromycin 500–600 mg + ethambutol 15 mg/kg) PO daily (AII) if drug interaction or intolerance precludes the use of clarithromycin <p><u>Duration:</u></p> <ul style="list-style-type: none"> • At least 12 months of therapy, can discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/μL in response to ART 	<p>Addition of a third or fourth drug should be considered for patients with advanced immunosuppression (CD4 counts <50 cells/μL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (CIII).</p> <p><u>Third or Fourth Drug Options May Include:</u></p> <ul style="list-style-type: none"> • RFB 300 mg PO daily (dosage adjustment may be necessary based on drug interactions) (CI), • Amikacin 10–15 mg/kg IV daily (CIII) or Streptomycin 1 g IV or IM daily (CIII)], <i>or</i> • Moxifloxacin 400 mg PO daily (CIII) or Levofloxacin 500 mg PO daily (CIII) 	<p>Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII).</p> <p>NSAIDs can be used for patients who experience moderate to severe symptoms attributed to IRIS (CIII).</p> <p>If IRIS symptoms persist, short-term (4–8 weeks) systemic corticosteroids (equivalent to 20–40 mg prednisone) can be used (CII).</p>
Bacterial Respiratory Diseases (with focus on pneumonia)	<p>Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII).</p> <p><u>Empiric Outpatient Therapy:</u></p> <ul style="list-style-type: none"> • A PO beta-lactam + a PO macrolide (azithromycin or clarithromycin) (AII) <ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> high-dose amoxicillin or amoxicillin/clavulanate • <i>Alternative beta-lactams:</i> cefpodoxime or cefuroxime, <i>or</i> • <i>For penicillin-allergic patients:</i> Levofloxacin 750 mg PO once daily (AII), or moxifloxacin 400 mg PO once daily (AII) <p><u>Duration:</u> 7–10 days (a minimum of 5 days). Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics.</p> <p><u>Empiric Therapy for Non-ICU Hospitalized Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + a macrolide (azithromycin or clarithromycin) (AII) 	<p><u>Empiric Outpatient Therapy:</u></p> <ul style="list-style-type: none"> • A PO beta-lactam + PO doxycycline (CIII) <ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> high-dose amoxicillin or amoxicillin/clavulanate • <i>Alternative beta-lactams:</i> cefpodoxime or cefuroxime <p><u>Empiric Therapy for Non-ICU Hospitalized Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + doxycycline (CIII) <p><u>Empiric Therapy For ICU Patients:</u></p> <ul style="list-style-type: none"> • <i>For penicillin-allergic patients:</i> Aztreonam IV + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII) <p><u>Empiric Therapy for Patients at Risk of <i>Pseudomonas</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • An IV antipseudomonal beta-lactam + an aminoglycoside + azithromycin (BIII), <i>or</i> 	<p>Fluoroquinolones should be used with caution in patients in whom TB is suspected but is not being treated.</p> <p>Empiric therapy with a macrolide alone is not routinely recommended, because of increasing pneumococcal resistance (BIII).</p> <p>Patients receiving a macrolide for MAC prophylaxis should not receive macrolide monotherapy for empiric treatment of bacterial pneumonia.</p> <p>For patients begun on IV antibiotic therapy, switching to PO should be considered when they are clinically improved and able to tolerate oral medications.</p> <p>Chemoprophylaxis can be considered for patients with frequent recurrences of serious bacterial pneumonia (CIII).</p> <p>Clinicians should be cautious about using antibiotics to prevent recurrences because of the potential for developing drug resistance and drug toxicities.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 6 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bacterial Respiratory Diseases <i>(with focus on pneumonia), continued</i>	<ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> ceftriaxone, cefotaxime, or ampicillin-sulbactam • <i>For penicillin-allergic patients:</i> Levofloxacin, 750 mg IV once daily (AII), or moxifloxacin, 400 mg IV once daily (AII) <p><u>Empiric Therapy for ICU Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + IV azithromycin (AII), <i>or</i> • An IV beta-lactam + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (AII) • <i>Preferred beta-lactams:</i> ceftriaxone, cefotaxime, or ampicillin-sulbactam <p><u>Empiric Therapy for Patients at Risk of <i>Pseudomonas</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • An IV antipneumococcal, antipseudomonal beta-lactam + (ciprofloxacin 400 mg IV q8–12h or levofloxacin 750 mg IV once daily) (BIII) • <i>Preferred beta-lactams:</i> piperacillin-tazobactam, cefepime, imipenem, or meropenem <p><u>Empiric Therapy for Patients at Risk for Methicillin-Resistant <i>Staphylococcus aureus</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • Add vancomycin IV or linezolid (IV or PO) to the baseline regimen (BIII). • Addition of clindamycin to vancomycin (but not to linezolid) can be considered for severe necrotizing pneumonia to minimize bacterial toxin production (CIII). 	<ul style="list-style-type: none"> • Above beta-lactam + an aminoglycoside + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII), <i>or</i> • <i>For penicillin-allergic patients:</i> Replace the beta-lactam with aztreonam (BIII). 	

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 7 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bacterial Enteric Infections: <i>Empiric Therapy pending definitive diagnosis.</i>	<p>Diagnostic fecal specimens should be obtained before initiation of empiric antibiotic therapy.</p> <p>Empiric antibiotic therapy is indicated for patients with advanced HIV (CD4 count <200 cells/μL or concomitant AIDS-defining illnesses), with clinically severe diarrhea (>6 stools/day) and/or accompanying fever or chills.</p> <p><u>Empiric Therapy:</u></p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII) <p>Therapy should be adjusted based on the results of diagnostic work-up.</p> <p>For patients with chronic diarrhea (>14 days) without severe clinical signs, empiric antibiotics therapy is not necessary, can withhold treatment until a diagnosis is made.</p>	<p><u>Empiric Therapy:</u></p> <ul style="list-style-type: none"> • Ceftriaxone 1 g IV q24h (BIII), <i>or</i> • Cefotaxime 1 g IV q8h (BIII) 	<p>Hospitalization with IV antibiotics should be considered in patients with marked nausea, vomiting, diarrhea, electrolyte abnormalities, acidosis, and blood pressure instability.</p> <p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided if there is concern about inflammatory diarrhea, including <i>Clostridium-difficile</i>-associated diarrhea (BIII).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture with antibiotic susceptibility testing or alternative diagnostic tests (e.g., toxin assays, molecular testing), alternative diagnosis, or antibiotic resistance.</p>
Salmonellosis	<p>All HIV-infected patients with salmonellosis should be treated because of high risk of bacteremia. (AIII)</p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h, if susceptible (AIII) <p><u>Duration of Therapy:</u></p> <p><i>For gastroenteritis without bacteremia:</i></p> <ul style="list-style-type: none"> • If CD4 count ≥200 cells/μL: 7–14 days (BIII) • If CD4 count <200 cells/μL: 2–6 weeks (CIII) <p><i>For gastroenteritis with bacteremia:</i></p> <ul style="list-style-type: none"> • If CD4 count ≥200/μL: 14 days (AIII); longer duration if bacteremia persists or if the infection is complicated (e.g., if metastatic foci of infection are present) (BIII) • If CD4 count <200 cells/μL: 2–6 weeks (BIII) <p><u>Secondary Prophylaxis Should Be Considered For:</u></p> <ul style="list-style-type: none"> • Patients with recurrent <i>Salmonella</i> gastroenteritis +/- bacteremia (CIII), <i>or</i> • Patients with CD4 <200 cells/μL with severe diarrhea (CIII) 	<ul style="list-style-type: none"> • Levofloxacin 750 mg (PO or IV) q24h (BIII), <i>or</i> • Moxifloxacin 400 mg (PO or IV) q24h (BIII), <i>or</i> • TMP, 160 mg-SMX 800 mg (PO or IV) q12h (BIII), <i>or</i> • Ceftriaxone 1 g IV q24h (BIII), <i>or</i> • Cefotaxime 1 g IV q8h (BIII) 	<p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>The role of long-term secondary prophylaxis in patients with recurrent <i>Salmonella</i> bacteremia is not well established. Must weigh benefit against risks of long-term antibiotic exposure (CIII).</p> <p>Effective ART may reduce the frequency, severity, and recurrence of salmonella infections.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 8 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Shigellosis	<ul style="list-style-type: none"> Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII) <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> <i>Gastroenteritis</i>: 7–10 days (AIII) <i>Bacteremia</i>: ≥ 14 days (BIII) <i>Recurrent Infections</i>: up to 6 weeks (BIII) 	<ul style="list-style-type: none"> Levofloxacin 750 mg (PO or IV) q24h (BIII), <i>or</i> Moxifloxacin 400 mg (PO or IV) q24h (BIII), <i>or</i> TMP 160 mg-SMX 800 mg (PO or IV) q12h (BIII) (Note: <i>Shigella</i> infections acquired outside of the United States have high rates of TMP-SMX resistance), <i>or</i> Azithromycin 500 mg PO daily for 5 days (BIII) (Note: not recommended for patients with bacteremia (AIII)) 	<p>Therapy is indicated both to shorten duration of illness and prevent spread of infection (AIII).</p> <p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>Effective ART may reduce the frequency, severity, and recurrence of <i>shigella</i> infections.</p>
Campylobacteriosis	<p><u>For Mild Disease and If CD4 Count >200 cells/μL:</u></p> <ul style="list-style-type: none"> Withhold therapy and monitor (CIII) <p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII), <i>or</i> Azithromycin 500 mg PO daily (BIII) (Note: Not for patients with bacteremia) <p><u>For <i>Campylobacter</i> Bacteremia:</u></p> <ul style="list-style-type: none"> Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII) + an aminoglycoside (BIII). <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> <i>Gastroenteritis</i>: 7–10 days (AIII) (5 days with azithromycin) <i>Bacteremia</i>: ≥ 14 days (BIII) <i>Recurrent bacteremia</i>: 2–6 weeks (BIII) 	<p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> Levofloxacin 750 mg (PO or IV) q24h (BIII), <i>or</i> Moxifloxacin 400 mg (PO or IV) q24h (BIII) <p>Add an aminoglycoside to fluoroquinolone in bacteremic patients (BIII).</p>	<p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>There is an increasing rate of fluoroquinolone resistance in the United States (22% resistance in 2009).</p> <p>Antimicrobial therapy should be modified based on susceptibility reports.</p> <p>Effective ART may reduce the frequency, severity, and recurrence of campylobacter infections.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 9 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bartonellosis	<p><u>For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, and Osteomyelitis:</u></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO or IV q12h (AII), <i>or</i> • Erythromycin 500 mg PO or IV q6h (AII) <p><u>CNS Infections:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg +/- RIF 300 mg) PO or IV q12h (AIII) <p><u>Confirmed <i>Bartonella</i> Endocarditis:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg IV q12h + gentamicin 1 mg/kg IV q8h) for 2 weeks, then continue with doxycycline 100 mg IV or PO q12h (BII) <p><u>Other Severe Infections:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg PO or IV +/- RIF 300 mg PO or IV) q12h (BIII), <i>or</i> • (Erythromycin 500 mg PO or IV q6h) +/- RIF 300 mg PO or IV q12h (BIII) <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> • At least 3 months (AII) 	<p><u>For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, And Osteomyelitis:</u></p> <ul style="list-style-type: none"> • Azithromycin 500 mg PO daily (BIII) • Clarithromycin 500 mg PO BID (BIII) <p><u>Confirmed <i>Bartonella</i> Endocarditis but with Renal Insufficiency:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg IV + RIF 300 mg PO or IV) q12h for 2 weeks, then continue with doxycycline 100 mg IV or PO q12h (BII) 	<p>When RIF is used, take into consideration the potential for significant interaction with ARV drugs and other medications (see Table 5 for dosing recommendations).</p> <p>If relapse occurs after initial (>3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 count <200 cells/μL (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 10 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Syphilis (<i>Treponema pallidum</i> Infection)	<p><u>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM for 1 dose (AII) <p><u>Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) <p><u>Late-Stage (Tertiary–Cardiovascular or Gummatous Disease):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) (Note: rule out neurosyphilis before initiation of benzathine penicillin, and obtain infectious diseases consultation to guide management) <p><u>Neurosyphilis (Including Otic or Ocular Disease):</u></p> <ul style="list-style-type: none"> • Aqueous crystalline penicillin G 18–24 million units per day (administered as 3–4 million units IV q4h or by continuous IV infusion) for 10–14 days (AII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of IV therapy (CIII) 	<p><u>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</u></p> <p><i>For penicillin-allergic patients</i></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 14 days (BII), or • Ceftriaxone 1 g IM or IV daily for 10–14 days (BII), or • Azithromycin 2 g PO for 1 dose (BII) (Note: azithromycin is not recommended for men who have sex with men or pregnant women (AII)) <p><u>Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):</u></p> <p><i>For penicillin-allergic patients</i></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 28 days (BIII) <p><u>Neurosyphilis:</u></p> <ul style="list-style-type: none"> • Procaine penicillin 2.4 million units IM daily plus probenecid 500 mg PO QID for 10–14 days (BII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of above (CIII), or • <i>For penicillin-allergic patients:</i> Desensitization to penicillin is the preferred approach (BIII); if not feasible, ceftriaxone, 2 g IV daily for 10–14 days (BII) 	<p>The efficacy of non-penicillin alternatives has not been evaluated in HIV-infected patients and they should be used only with close clinical and serologic monitoring.</p> <p>Combination of procaine penicillin and probenecid is not recommended for patients who are allergic to sulfa-containing medications (AIII).</p> <p>The Jarisch-Herxheimer reaction is an acute febrile reaction accompanied by headache and myalgia that can occur within the first 24 hours after therapy for syphilis. This reaction occurs most frequently in patients with early syphilis, high non-treponemal titers, and prior penicillin treatment.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 11 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Mucocutaneous candidiasis	<p><u>For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):</u></p> <p><i>Oral Therapy</i></p> <ul style="list-style-type: none"> • Fluconazole 100 mg PO daily (AI), <i>or</i> <p><i>Topical Therapy</i></p> <ul style="list-style-type: none"> • Clotrimazole troches, 10 mg PO 5 times daily (BI), <i>or</i> • Miconazole mucoadhesive buccal 50-mg tablet—apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush) (BI) <p><u>For Esophageal Candidiasis (For 14–21 Days):</u></p> <ul style="list-style-type: none"> • Fluconazole 100 mg (up to 400 mg) PO or IV daily (AI), <i>or</i> • Itraconazole oral solution 200 mg PO daily (AI) <p><u>For Uncomplicated Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> • Oral fluconazole 150 mg for 1 dose (AII), <i>or</i> • Topical azoles (clotrimazole, butoconazole, miconazole, tioconazole, or terconazole) for 3–7 days (AII) <p><u>For Severe or Recurrent Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> • Fluconazole 100–200 mg PO daily for ≥7 days (AII), <i>or</i> • Topical antifungal ≥7 days (AII) 	<p><u>For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):</u></p> <p><i>Oral Therapy</i></p> <ul style="list-style-type: none"> • Itraconazole oral solution 200 mg PO daily (BI), <i>or</i> • Posaconazole oral solution 400 mg PO BID for 1 day, then 400 mg daily (BI) <p><i>Topical Therapy</i></p> <ul style="list-style-type: none"> • Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily (BII) <p><u>For Esophageal Candidiasis (For 14–21 Days):</u></p> <ul style="list-style-type: none"> • Voriconazole 200 mg PO or IV BID (BI), <i>or</i> • Posaconazole 400 mg PO BID (BI), <i>or</i> • Anidulafungin 100 mg IV 1 time, then 50 mg IV daily (BI), <i>or</i> • Caspofungin 50 mg IV daily (BI), <i>or</i> • Micafungin 150 mg IV daily (BI), <i>or</i> • Amphotericin B deoxycholate 0.6 mg/kg IV daily (BI), <i>or</i> • Lipid formulation of amphotericin B 3–4 mg/kg IV daily (BIII) <p><u>For Uncomplicated Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> • Itraconazole oral solution 200 mg PO daily for 3–7 days (BII) 	<p>Chronic or prolonged use of azoles may promote development of resistance.</p> <p>Higher relapse rate for esophageal candidiasis seen with echinocandins than with fluconazole use.</p> <p>Suppressive therapy usually not recommended (BIII) unless patients have frequent or severe recurrences.</p> <p><u>If Decision Is to Use Suppressive Therapy:</u></p> <p><i>Oropharyngeal candidiasis:</i></p> <ul style="list-style-type: none"> • Fluconazole 100 mg PO daily or TIW (BI) • Itraconazole oral solution 200 mg PO daily (CI) <p><i>Esophageal candidiasis:</i></p> <ul style="list-style-type: none"> • Fluconazole 100–200 mg PO daily (BI) • Posaconazole 400 mg PO BID (BII) <p><i>Vulvo-vaginal candidiasis:</i></p> <ul style="list-style-type: none"> • Fluconazole 150 mg PO once weekly (CII)

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 12 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cryptococcosis	<p><u>Cryptococcal Meningitis</u></p> <p><i>Induction Therapy (for at least 2 weeks, followed by consolidation therapy):</i></p> <ul style="list-style-type: none"> Liposomal amphotericin B 3–4 mg/kg IV daily + flucytosine 25 mg/kg PO QID (AI) (Note: Flucytosine dose should be adjusted in patients with renal dysfunction.) <p><i>Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):</i></p> <ul style="list-style-type: none"> Fluconazole 400 mg PO (or IV) daily (AI) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> Fluconazole 200 mg PO daily for at least 12 months (AI) <p><u>For Non-CNS, Extrapulmonary Cryptococcosis and Diffuse Pulmonary Disease:</u></p> <ul style="list-style-type: none"> Treatment same as for cryptococcal meningitis (BIII) <p><u>Non-CNS Cryptococcosis with Mild-to-Moderate Symptoms and Focal Pulmonary Infiltrates:</u></p> <ul style="list-style-type: none"> Fluconazole, 400 mg PO daily for 12 months (BIII) 	<p><u>Cryptococcal meningitis</u></p> <p><i>Induction Therapy (for at least 2 weeks, followed by consolidation therapy):</i></p> <ul style="list-style-type: none"> Amphotericin B deoxycholate 0.7 mg/kg IV daily + flucytosine 25 mg/kg PO QID (AI), or Amphotericin B lipid complex 5 mg/kg IV daily + flucytosine 25 mg/kg PO QID (BII), or Liposomal amphotericin B 3–4 mg/kg IV daily + fluconazole 800 mg PO or IV daily (BIII), or Amphotericin B deoxycholate 0.7 mg/kg IV daily + fluconazole 800 mg PO or IV daily (BI), or Fluconazole 400–800 mg PO or IV daily + flucytosine 25 mg/kg PO QID (BII), or Fluconazole 1200 mg PO or IV daily (CII) <p><i>Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO BID for 8 weeks—less effective than fluconazole (CI) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> No alternative therapy recommendation 	<p>Addition of flucytosine to amphotericin B has been associated with more rapid sterilization of CSF and decreased risk for subsequent relapse.</p> <p>Patients receiving flucytosine should have either blood levels monitored (peak level 2 hours after dose should be 30–80 mcg/mL) or close monitoring of blood counts for development of cytopenia. Dosage should be adjusted in patients with renal insufficiency (BII).</p> <p>Opening pressure should always be measured when an LP is performed (AII). Repeated LPs or CSF shunting are essential to effectively manage increased intracranial pressure (BIII).</p> <p>Corticosteroids and mannitol are ineffective in reducing ICP and are NOT recommended (BII).</p> <p>Some specialists recommend a brief course of corticosteroid for management of severe IRIS symptoms (CIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 13 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Histoplasmosis	<p><u>Moderately Severe to Severe Disseminated Disease</u></p> <p><i>Induction Therapy (for at least 2 weeks or until clinically improved):</i></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 3 mg/kg IV daily (AI) <p><i>Maintenance Therapy</i></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (AII) <p><u>Less Severe Disseminated Disease</u></p> <p><i>Induction and Maintenance Therapy:</i></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (AII) <p><i>Duration of Therapy:</i></p> <ul style="list-style-type: none"> • At least 12 months <p><u>Meningitis</u></p> <p><i>Induction Therapy (4–6 weeks):</i></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 5 mg/kg/day (AIII) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO BID to TID for ≥1 year and until resolution of abnormal CSF findings (AII) <p><u>Long-Term Suppression Therapy:</u></p> <p><i>For patients with severe disseminated or CNS infection (AIII) after completion of at least 12 months of therapy; and those who relapse despite appropriate therapy (BIII):</i></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO daily (AIII) 	<p><u>Moderately Severe to Severe Disseminated Disease</u></p> <p><i>Induction Therapy (for at least 2 weeks or until clinically improved):</i></p> <ul style="list-style-type: none"> • Amphotericin B lipid complex 3 mg/kg IV daily (AIII), or • Amphotericin B cholesteryl sulfate complete 3 mg/kg IV daily (AIII) <p><u>Alternatives to Itraconazole for Maintenance Therapy or Treatment of Less Severe Disease:</u></p> <ul style="list-style-type: none"> • Voriconazole 400 mg PO BID for 1 day, then 200 mg BID (BIII), or • Posaconazole 400 mg PO BID (BIII) • Fluconazole 800 mg PO daily (CII) <p><u>Meningitis:</u></p> <ul style="list-style-type: none"> • No alternative therapy recommendation <p><u>Long-Term Suppression Therapy:</u></p> <ul style="list-style-type: none"> • Fluconazole 400 mg PO daily (BIII) 	<p>Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations.</p> <p>Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities.</p> <p>Random serum concentration of itraconazole + hydroitraconazole should be >1 µg/mL.</p> <p>Clinical experience with voriconazole or posaconazole in the treatment of histoplasmosis is limited.</p> <p>Acute pulmonary histoplasmosis in HIV-infected patients with CD4 counts >300 cells/µL should be managed as non-immunocompromised host (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 14 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Coccidioidomycosis	<p><u>Clinically Mild Infections (e.g., Focal Pneumonia):</u></p> <ul style="list-style-type: none"> Fluconazole 400 mg PO daily (BII), <i>or</i> Itraconazole 200 mg PO BID (BII) <p><u>Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):</u></p> <ul style="list-style-type: none"> Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (AII) Lipid formulation amphotericin B 4–6 mg/kg IV daily (AIII) Duration of therapy: continue until clinical improvement, then switch to an azole (BIII) <p><u>Meningeal Infections:</u></p> <ul style="list-style-type: none"> Fluconazole 400–800 mg IV or PO daily (AII) <p><u>Chronic Suppressive Therapy:</u></p> <ul style="list-style-type: none"> Fluconazole 400 mg PO daily (AII), <i>or</i> Itraconazole 200 mg PO BID (AII) 	<p><u>Mild Infections (Focal Pneumonia)</u> <i>For Patients Who Failed to Respond to Fluconazole or Itraconazole:</i></p> <ul style="list-style-type: none"> Posaconazole 200 mg PO BID (BII), <i>or</i> Voriconazole 200 mg PO BID (BIII) <p><u>Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):</u></p> <ul style="list-style-type: none"> Some specialists will add a triazole (fluconazole or itraconazole, with itraconazole preferred for bone disease) 400 mg per day to amphotericin B therapy and continue triazole once amphotericin B is stopped (BIII). <p><u>Meningeal Infections:</u></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (BII), <i>or</i> Posaconazole 200 mg PO BID (BIII), <i>or</i> Voriconazole 200–400 mg PO BID (BIII), <i>or</i> Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (AIII) <p><u>Chronic Suppressive Therapy:</u></p> <ul style="list-style-type: none"> Posaconazole 200 mg PO BID (BII), <i>or</i> Voriconazole 200 mg PO BID (BIII) 	<p>Some patients with meningitis may develop hydrocephalus and require CSF shunting.</p> <p>Therapy should be continued indefinitely in patients with diffuse pulmonary or disseminated diseases because relapse can occur in 25%–33% of HIV-negative patients. It can also occur in HIV-infected patients with CD4 counts >250 cells/μL (BIII).</p> <p>Therapy should be lifelong in patients with meningeal infections because relapse occurs in 80% of HIV-infected patients after discontinuation of triazole therapy (AII).</p> <p>Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations. Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and antiretroviral efficacy and reduce concentration-related toxicities.</p> <p>Intrathecal amphotericin B should only be given in consultation with a specialist and administered by an individual with experience with the technique.</p>
Aspergillosis, invasive	<p><u>Preferred Therapy:</u></p> <ul style="list-style-type: none"> Voriconazole 6 mg/kg IV q12h for 1 day, then 4 mg/kg IV q12h, followed by voriconazole 200 mg PO q12h after clinical improvement (AI) <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> Until CD4 cell count >200 cells/μL and the infection appears to be resolved (BIII) 	<p><u>Alternative Therapy:</u></p> <ul style="list-style-type: none"> Lipid formulation of amphotericin B 5 mg/kg IV daily (AII), <i>or</i> Amphotericin B deoxycholate 1mg/kg IV daily (AII), <i>or</i> Caspofungin 70 mg IV 1 time, then 50 mg IV daily (BIII), <i>or</i> Micafungin 100–150 mg IV daily (BIII), <i>or</i> Anidulafungin 200 mg IV 1 time, then 100 mg IV daily (BIII), <i>or</i> Posaconazole 200 mg PO QID, then, after condition improved, 400 mg PO BID (BII) 	<p>Potential for significant pharmacokinetic interactions between certain ARV agents and voriconazole; they should be used cautiously in these situations. Consider therapeutic drug monitoring and dosage adjustment if necessary.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 15 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cytomegalovirus (CMV) Disease	<p><u>CMV Retinitis</u> <u>Induction Therapy:</u> <i>For Immediate Sight-Threatening Lesions (Adjacent to the Optic Nerve or Fovea):</i></p> <ul style="list-style-type: none"> Intravitreal injections of ganciclovir (2mg) or foscarnet (2.4mg) for 1-4 doses over a period of 7-10 days to achieve high intraocular concentration faster (AIII); Plus one of the listed preferred or alternative systemic therapy: <p><i>Preferred Systemic Induction Therapy:</i></p> <ul style="list-style-type: none"> Valganciclovir 900 mg PO BID for 14–21 days (AI) <p><i>For Peripheral Lesions</i> – Administer one of the preferred or alternative systemic therapy</p> <p><u>Chronic Maintenance (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> Valganciclovir 900 mg PO daily (AI) <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h; may switch to valganciclovir 900 mg PO q12h once the patient can tolerate oral therapy (BI) Duration: 21–42 days or until symptoms have resolved (CII) Maintenance therapy is usually not necessary, but should be considered after relapses (BII). <p><u>Well-Documented, Histologically Confirmed CMV Pneumonia:</u></p> <ul style="list-style-type: none"> Experience for treating CMV pneumonitis in HIV patients is limited. Use of IV ganciclovir or IV foscarnet is reasonable (doses same as for CMV retinitis) (CIII). The optimal duration of therapy and the role of oral valganciclovir have not been established. <p><u>CMV Neurological Disease</u> Note: Treatment should be initiated promptly.</p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h + (foscarnet 90 mg/kg IV q12h or 60 mg/kg IV q8h) to stabilize disease 	<p><u>CMV Retinitis</u> <u>Alternative Systemic Induction Therapy:</u></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h for 14–21 days (AI), or Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h for 14–21 days (AI), or Cidofovir 5 mg/kg/week IV for 2 weeks; saline hydration before and after therapy and probenecid, 2 g PO 3 hours before dose, followed by 1 g PO 2 hours and 8 hours after the dose (total of 4 g) (BI). (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.) <p><i>Chronic Maintenance (Secondary Prophylaxis):</i></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV 5–7 times weekly (AI), or Foscarnet 90–120 mg/kg IV once daily (AI), or Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above (BI) <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h (BI) for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, or Valganciclovir 900 mg PO q12h in milder disease and if able to tolerate PO therapy (BII), or For mild cases, if ART can be initiated without delay, consider withholding CMV therapy (CIII). Duration: 21–42 days or until symptoms have resolved (CII) 	<p>The choice of therapy for CMV retinitis should be individualized, based on location and severity of the lesions, level of immunosuppression, and other factors (e.g., concomitant medications and ability to adhere to treatment) (AIII).</p> <p>The ganciclovir ocular implant, which is effective for treatment of CMV retinitis is no longer available. For sight threatening retinitis, intravitreal injections of ganciclovir or foscarnet can be given to achieve higher ocular concentration faster.</p> <p>The choice of chronic maintenance therapy (route of administration and drug choices) should be made in consultation with an ophthalmologist. Considerations should include the anatomic location of the retinal lesion, vision in the contralateral eye, the patients' immunologic and virologic status and response to ART.</p> <p>Patients with CMV retinitis who discontinue maintenance therapy should undergo regular eye examinations—optimally every 3 months—for early detection of relapse IRU, and then annually after immune reconstitution (AIII).</p> <p>IRU may develop in the setting of immune reconstitution.</p> <p><u>Treatment of IRU</u></p> <ul style="list-style-type: none"> Periocular corticosteroid or short courses of systemic steroid (BIII). <p>Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART (BIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 16 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cytomegalovirus (CMV) Disease, continued	<p>and maximize response, continue until symptomatic improvement and resolution of neurologic symptoms (CIII)</p> <ul style="list-style-type: none"> The optimal duration of therapy and the role of oral valganciclovir have not been established. 		
Herpes Simplex Virus (HSV) Disease	<p><u>Oral Labial Lesions (For 5–10 Days):</u></p> <ul style="list-style-type: none"> Valacyclovir 1 g PO BID (AIII), <i>or</i> Famciclovir 500 mg PO BID (AIII), <i>or</i> Acyclovir 400 mg PO TID (AIII) <p><u>Initial or Recurrent Genital HSV (For 5–14 Days):</u></p> <ul style="list-style-type: none"> Valacyclovir 1 g PO BID (AI), <i>or</i> Famciclovir 500 mg PO BID (AI), <i>or</i> Acyclovir 400 mg PO TID (AI) <p><u>Severe Mucocutaneous HSV:</u></p> <ul style="list-style-type: none"> Initial therapy acyclovir 5 mg/kg IV q8h (AIII) After lesions begin to regress, change to PO therapy as above. Continue until lesions are completely healed. <p><u>Chronic Suppressive Therapy</u></p> <p><i>For patients with severe recurrences of genital herpes (AI) or patients who want to minimize frequency of recurrences (AI):</i></p> <ul style="list-style-type: none"> Valacyclovir 500 mg PO BID (AI) Famciclovir 500 mg PO BID (AI) Acyclovir 400 mg PO BID (AI) Continue indefinitely regardless of CD4 cell count. 	<p><u>For Acyclovir-Resistant HSV</u></p> <p><i>Preferred Therapy:</i></p> <ul style="list-style-type: none"> Foscarnet 80–120 mg/kg/day IV in 2–3 divided doses until clinical response (AI) <p><i>Alternative Therapy (CIII):</i></p> <ul style="list-style-type: none"> IV cidofovir (dosage as in CMV retinitis), <i>or</i> Topical trifluridine, <i>or</i> Topical cidofovir, <i>or</i> Topical imiquimod <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> 21–28 days or longer 	<p>Patients with HSV infections can be treated with episodic therapy when symptomatic lesions occur, or with daily suppressive therapy to prevent recurrences.</p> <p>Topical formulations of trifluridine and cidofovir are not commercially available.</p> <p>Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic solution and the IV formulation of cidofovir.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 17 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Varicella Zoster Virus (VZV) Disease	<p><u>Primary Varicella Infection (Chickenpox)</u></p> <p><i>Uncomplicated Cases (For 5–7 Days):</i></p> <ul style="list-style-type: none"> • Valacyclovir 1 g PO TID (AII), or • Famciclovir 500 mg PO TID (AII) <p><i>Severe or Complicated Cases:</i></p> <ul style="list-style-type: none"> • Acyclovir 10–15 mg/kg IV q8h for 7–10 days (AIII) • May switch to oral valacyclovir, famciclovir, or acyclovir after defervescence if no evidence of visceral involvement (BIII). <p><u>Herpes Zoster (Shingles)</u></p> <p><i>Acute Localized Dermatomal:</i></p> <ul style="list-style-type: none"> • For 7–10 days; consider longer duration if lesions are slow to resolve • Valacyclovir 1 g PO TID (AII), or • Famciclovir 500 mg TID (AII) <p><i>Extensive Cutaneous Lesion or Visceral Involvement:</i></p> <ul style="list-style-type: none"> • Acyclovir 10–15 mg/kg IV q8h until clinical improvement is evident (AII) • May switch to PO therapy (valacyclovir, famciclovir, or acyclovir) after clinical improvement (i.e., when no new vesicle formation or improvement of signs and symptoms of visceral VZV), to complete a 10–14 day course (BIII). <p><u>Progressive Outer Retinal Necrosis (PORN):</u></p> <ul style="list-style-type: none"> • (Ganciclovir 5 mg/kg +/- foscarnet 90 mg/kg) IV q12h + (ganciclovir 2 mg/0.05mL +/- foscarnet 1.2 mg/0.05 mL) intravitreal injection BIW (AIII) • Initiate or optimize ART (AIII) <p><u>Acute Retinal Necrosis (ARN):</u></p> <ul style="list-style-type: none"> • (Acyclovir 10–15 mg/kg IV q8h) + (ganciclovir 2 mg/0.05mL intravitreal injection BIW X 1–2 doses) for 10–14 days, followed by valacyclovir 1g PO TID for 6 weeks (AIII) 	<p><u>Primary Varicella Infection (Chickenpox)</u></p> <p><i>Uncomplicated Cases (For 5–7 Days):</i></p> <ul style="list-style-type: none"> • Acyclovir 800 mg PO 5 times/day (BII) <p><u>Herpes Zoster (Shingles)</u></p> <p><i>Acute Localized Dermatomal:</i></p> <ul style="list-style-type: none"> • For 7–10 days; consider longer duration if lesions are slow to resolve • Acyclovir 800 mg PO 5 times/day (BII) 	<p>In managing VZV retinitis - Consultation with an ophthalmologist experienced in management of VZV retinitis is strongly recommended (AIII).</p> <p>Duration of therapy for VZV retinitis is not well defined, and should be determined based on clinical, virologic, and immunologic responses and ophthalmologic responses.</p> <p>Optimization of ART is recommended for serious and difficult-to-treat VZV infections (e.g., retinitis, encephalitis) (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 18 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments		
HHV-8 Diseases (Kaposi Sarcoma [KS], Primary Effusion Lymphoma [PEL], Multicentric Castleman's Disease [MCD])	<p>Mild To Moderate KS (ACTG Stage T0):</p> <ul style="list-style-type: none">Initiate or optimize ART (AII) <p>Advanced KS [ACTG Stage T1, Including Disseminated Cutaneous (AI) Or Visceral KS (BIII)]:</p> <ul style="list-style-type: none">Chemotherapy (per oncology consult) + ART <p>Primary Effusion Lymphoma:</p> <ul style="list-style-type: none">Chemotherapy (per oncology consult) + ART (AI)PO valganciclovir or IV ganciclovir can be used as adjunctive therapy (CIII). <p>MCD:</p> <ul style="list-style-type: none">Valganciclovir 900 mg PO BID for 3 weeks (CII), orGanciclovir 5 mg/kg IV q12h for 3 weeks (CII), orValganciclovir 900 mg PO BID + zidovudine 600 mg PO q6h for 7–21 days (CII)	<p>MCD</p> <ul style="list-style-type: none">Rituximab (375 mg/m² given weekly for 4–8 weeks) may be an alternative to or used adjunctively with antiviral therapy (CII).	<ul style="list-style-type: none">Patients who received rituximab for MCD may experience subsequent exacerbation or emergence of KS		
Human Papillomavirus (HPV) Disease	<p>Treatment of Condyloma Acuminata (Genital Warts)</p> <table><tr><td><p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p><ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID for 3 consecutive days, followed by 4 days of no therapy, repeat weekly for up to 4 cycles, until lesions are no longer visible (BIII), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).</td><td><p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient Applied Therapy:</u></p><ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (BIII), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).</td></tr></table>		<p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p> <ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID for 3 consecutive days, followed by 4 days of no therapy, repeat weekly for up to 4 cycles, until lesions are no longer visible (BIII), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).	<p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient Applied Therapy:</u></p> <ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (BIII), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).	<p>HIV-infected patients may have larger or more numerous warts and may not respond as well to therapy for genital warts when compared to HIV-uninfected individuals.</p> <p>Topical cidofovir has activity against genital warts, but the product is not commercially available (CIII).</p> <p>Intralesional interferon-alpha is usually not recommended because of high cost, difficult administration, and potential for systemic side effects (CIII).</p> <p>The rate of recurrence of genital warts is high despite treatment in HIV-infected patients.</p> <p>There is no consensus on the treatment of oral warts. Many treatments for anogenital warts cannot be used in the oral mucosa. Surgery is the most common treatment for oral warts that interfere with function or for aesthetic reasons.</p>
<p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p> <ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID for 3 consecutive days, followed by 4 days of no therapy, repeat weekly for up to 4 cycles, until lesions are no longer visible (BIII), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).	<p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient Applied Therapy:</u></p> <ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (BIII), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).				

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 19 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Hepatitis B Virus (HBV) Disease	<p>ART is recommended for all HIV/HBV-co-infected patients regardless of CD4 cell count (AII).</p> <p>ART regimen should include 2 drugs that are active against both HBV and HIV, such as [tenofovir 300 mg + emtricitabine 200 mg (or lamivudine 300 mg)] PO once daily (+ additional drug(s) for HIV) (AIII).</p> <p><u>Duration:</u> Continue treatment indefinitely (CIII)</p>	<p><u>For Patients Who Refuse or Are Unable to Take ART:</u></p> <ul style="list-style-type: none"> Assess HBV disease stage and whether HBV treatment should be undertaken. If no indication for treatment of HBV infection, continue to monitor and reassess at a later time. <p>[HBV treatment is indicated for patients with active liver disease, elevated ALT and HBV DNA >2,000 international units/mL or significant liver fibrosis. (AI)], <i>or</i></p> <ul style="list-style-type: none"> Peginterferon alfa-2a 180 µg SQ weekly for 48 weeks (CIII), <i>or</i> Peginterferon alfa 2b 1.5 µg/kg SQ once weekly for 48 weeks (CIII) <p><u>If Tenofovir Cannot Be Used as Part of HIV/HBV Therapy (Because of Existing or High Risk of Renal Dysfunction):</u></p> <ul style="list-style-type: none"> Use a fully suppressive ART regimen with entecavir (dose adjustment according to renal function) (BIII). 	<p>Adefovir, emtricitabine, entecavir, lamivudine, telbivudine, or tenofovir should not be used for the treatment of HBV infection in patients who are not receiving combination ART (AII).</p> <p>Cross-resistance to emtricitabine or telbivudine should be assumed in patients with suspected or proven lamivudine-resistance.</p> <p>When changing ART regimens, continue agents with anti-HBV activity because of the risk of IRIS (AIII).</p> <p>If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted because it can be potentially life-saving (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 20 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Hepatitis C Virus (HCV) Disease	<p><u>Acute HCV Infection:</u></p> <ul style="list-style-type: none"> • Treatment should be offered (AII). Because of the high rate of spontaneous clearance, some experts recommend observation for 3–6 months before initiation of therapy, especially for patients with IL28B C/C genotype. • (PegIFN alfa-2a 180 µg or PegIFN alfa-2b 1.5 µg/kg) SQ weekly + RBV PO (dose according to HCV genotype—see below) (AII) • Duration of therapy: 24–48 weeks <p><u>Chronic HCV Infection</u></p> <p><u>Genotype 1:</u></p> <ul style="list-style-type: none"> • (PegIFN alfa-2a 180 µg or PegIFN alfa-2b 1.5 µg/kg) SQ weekly (AI) + RBV PO (weight-based dosing) (AI) <ul style="list-style-type: none"> • <75 kg: 600 mg qAM and 400 mg qPM; • ≥75 kg: 600 mg qAM and 600 mg qPM +/- BOC or TVR (based on ART—see next column) (BIII) <ul style="list-style-type: none"> • Total duration of therapy: 48 weeks (AI) <p><u>Genotype 2, 3, 4, 5, or 6 (AI):</u></p> <ul style="list-style-type: none"> • (PegIFN alfa-2a 180 µg or PegIFN alfa-2b 1.5 µg/kg) SQ weekly + RBV 400 mg PO BID • Duration of therapy: 48 weeks (AI) • Some experts recommend 24 weeks of therapy for patients who achieve an undetectable HCV RNA at treatment week 4, especially those who experience significant side effects (CIII). 	<p>In Patients for Whom RBV Is Contraindicated (Patients With Un-Modifiable Pre-Existing Anemia, or with Hemoglobinopathy):</p> <ul style="list-style-type: none"> • PegIFN alfa-2a 180 µg SQ weekly (AII), or • PegIFN alfa-2b 1.5 µg/kg SQ weekly (AII) <p><u>In Patients with Decompensated Liver Disease:</u></p> <ul style="list-style-type: none"> • Liver transplantation if feasible (CIII) <p><u>Recommendations for Use of BOC or TVR Patients Infected With HCV Genotype 1; Per ART Usage</u></p> <p><u>No ART or Receiving (RAL + 2 NRTI):</u></p> <ul style="list-style-type: none"> • BOC 800 mg PO TID (q7–9h) beginning after 4 weeks of PegIFN/RBV and continue for an additional 44 weeks, or • TVR 750 mg PO TID (q7–9h) for 12 weeks (with Peg IFN/RBV), then continue PegIFN/RBV (without TVR) for a total of 48 weeks) <p><u>ATV/r + 2 NRTI:</u></p> <ul style="list-style-type: none"> • TVR (+ Peg IFN/RBV, dose and duration as above) <p><u>EFV + 2 NRTI</u></p> <ul style="list-style-type: none"> • TVR 1125 mg PO TID for 12 weeks (+ PegIFN/RBV as stated above) <p><u>Receiving Other ART Regimens:</u></p> <ul style="list-style-type: none"> • Defer HCV treatment (especially in patients with no or minimal fibrosis) (BIII), or • Use Peg IFN/RBV without HCV PI (in patients with good prognosis, such as IL28B C/C genotype or low HCV RNA level (<400,000 international units/mL), or • If feasible, based on ARV history and HIV genotype testing, modify ART to one of the allowable regimens, monitor for at least 4 weeks for tolerability and efficacy, before starting HCV therapy, or • For patients with complex ART treatment history (e.g., multiple HIV drug resistances and/or toxicities), consult an expert for an optimal strategy for both HIV and HCV treatment (AIII). In some cases, TVR may be preferable because of shorter duration of therapy. 	<p>HCV treatment is generally not recommended in patients with CD4 count <200 cells/µL (CIII).</p> <p>ddI + RBV may lead to increased mitochondrial toxicities; concomitant use is contraindicated (AII).</p> <p>ZDV use with RBV +/- HCV PI may lead to increased anemia; concomitant use should be avoided (AII).</p> <p>HCV therapy is not recommended in patients with hepatic decompensation. Liver transplantation, if feasible, should be the primary treatment option (CIII).</p> <p>IFN is abortifacient in high doses and RBV is teratogenic. HCV treatment is not recommended in pregnant women or women who are not willing to use birth control (AIII).</p> <p>BOC and TVR are not recommended for non-genotype 1 HCV infections. BOC and TVR should not be given without RBV because of high likelihood of virologic failure (AI).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 21 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Progressive Multifocal Leukoencephalopathy (PML) (JC Virus Infections)	There is no specific antiviral therapy for JC virus infection. The main treatment approach is to reverse the immunosuppression caused by HIV. Initiate ART immediately in ART-naïve patients (AII) . Optimize ART in patients who develop PML in phase of HIV viremia on ART (AIII)	None.	Corticosteroids may be used for PML-IRIS characterized by contrast enhancement, edema or mass effect, and with clinical deterioration (BIII) (see text for further discussion).
Malaria	Because <i>Plasmodium falciparum</i> malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all HIV-infected patients with confirmed or suspected <i>P. falciparum</i> infection should be hospitalized for evaluation, initiation of treatment, and observation (AIII) . Treatment recommendations for HIV-infected patients are the same as HIV-uninfected patients (AIII) . Choice of therapy is guided by the degree of parasitemia, the species of <i>Plasmodium</i> , the patient's clinical status, region of infection, and the likely drug susceptibility of the infected species, and can be found at http://www.cdc.gov/malaria .	When suspicion for malaria is low, antimalarial treatment should not be initiated until the diagnosis is confirmed.	For treatment recommendations for specific regions, clinicians should refer to the following web link: http://www.cdc.gov/malaria/ or call the CDC Malaria Hotline: (770) 488-7788: M–F 8 AM–4:30 PM ET, or (770) 488-7100 after hours
Leishmaniasis, visceral	<u>For Initial Infection:</u> <ul style="list-style-type: none"> • Liposomal amphotericin B 2–4 mg/kg IV daily (AII), <i>or</i> • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) (AII) • To achieve total dose of 20–60 mg/kg (AII) <u>Chronic Maintenance Therapy (Secondary Prophylaxis): Especially in Patients with CD4 Count <200 cells/μL:</u> <ul style="list-style-type: none"> • Liposomal amphotericin B 4 mg/kg every 2–4 weeks (AII), <i>or</i> Amphotericin B lipid complex (AII) 3 mg/kg every 21 days (AII)	<u>For Initial Infection:</u> <ul style="list-style-type: none"> • Other lipid formulation of amphotericin B, dose and schedule as in Preferred Therapy, <i>or</i> • Amphotericin B deoxycholate 0.5–1.0 mg/kg IV daily for total dose of 1.5–2.0 g (BII), <i>or</i> • Sodium stibogluconate (pentavalent antimony) (BII) 20 mg/kg IV or IM daily for 28 days. <u>Another Option:</u> <ul style="list-style-type: none"> • Miltefosine 100 mg PO daily for 4 weeks (available in the United States under a treatment IND) (CIII) <u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u> Sodium stibogluconate 20 mg/kg IV or IM every 4 weeks (BII)	ART should be initiated or optimized (AIII) . For sodium stibogluconate, contact the CDC Drug Service at (404) 639-3670 or drugservice@cdc.gov .

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 22 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Leishmaniasis, cutaneous	<ul style="list-style-type: none"> • Liposomal amphotericin B 2–4 mg/kg IV daily for 10 days (BIII), <i>or</i> • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) to achieve total dose of 20–60 mg/kg (BIII), <i>or</i> • Sodium stibogluconate 20 mg/kg IV or IM daily for 3–4 weeks (BIII) <p><u>Chronic Maintenance Therapy:</u> May be indicated in immunocompromised patients with multiple relapses (CIII)</p>	<p><u>Possible Options Include:</u></p> <ul style="list-style-type: none"> • Oral miltefosine (can be obtained via a treatment IND), <i>or</i> • Topical paromomycin, <i>or</i> • Intralesional sodium stibogluconate, <i>or</i> • Local heat therapy <p>No data exist for any of these agents in HIV-infected patients; choice and efficacy dependent on species of <i>Leishmania</i>.</p>	None.
Chagas Disease (American Trypanosomiasis)	<p><u>For Acute, Early Chronic, and Re-Activated Disease:</u></p> <ul style="list-style-type: none"> • Benznidazole 5–8 mg/kg/day PO in 2 divided doses for 30–60 days (BIII) (not commercially available in the United States; contact the CDC Drug Service at drugservice@cdc.gov or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100) 	<p><u>For Acute, Early Chronic, And Reactivated Disease</u></p> <p>Nifurtimox 8–10 mg/kg/day PO for 90–120 days (CIII) (not commercially available in the U.S., contact the CDC Drug Service at drugservice@cdc.gov or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100)</p>	<p>Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. It is ineffective in achieving parasitological cure.</p> <p>Duration of therapy has not been studied in HIV-infected patients.</p> <p>Initiate or optimize ART in patients undergoing treatment for Chagas disease, once they are clinically stable (AIII).</p>
Penicilliosis marneffei	<p><u>For Acute Infection in Severely Ill Patients:</u></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 3–5 mg/kg/day IV for 2 weeks, followed by itraconazole 200 mg PO BID for 10 weeks (AII), followed by chronic maintenance therapy (as below) <p><u>For Mild Disease:</u></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO BID for 8 weeks (BII); followed by chronic maintenance therapy (as below) <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO daily (AI) 	<p><u>For Acute Infection in Severely Ill Patients:</u></p> <ul style="list-style-type: none"> • Voriconazole 6 mg/kg IV q12h for 1 day, then 4 mg/kg IV q12h for at least 3 days, followed by 200 mg PO BID for a maximum of 12 weeks (BII), followed by maintenance therapy <p><u>For Mild Disease:</u></p> <ul style="list-style-type: none"> • Voriconazole 400 mg PO BID for 1 day, then 200 mg BID for a maximum of 12 weeks (BII), followed by chronic maintenance therapy 	<p>ART should be initiated simultaneously with treatment for penicilliosis to improve treatment outcome (CIII).</p> <p>Itraconazole and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations.</p> <p>Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 23 of 23)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Isosporiasis	<p><u>For Acute Infection:</u></p> <ul style="list-style-type: none"> • TMP-SMX (160 mg/800 mg) PO (or IV) QID for 10 days (AII), <i>or</i> • TMP-SMX (160 mg/800 mg) PO (or IV) BID for 7–10 days (BI) • Can start with BID dosing first and increase daily dose and/or duration (up to 3–4 weeks) if symptoms worsen or persist (BIII) • IV therapy may be used for patients with potential or documented mal-absorption. <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • In patients with CD4 count <200/μL, TMP-SMX (160 mg/800 mg) PO TIW (AI) 	<p><u>For Acute Infection:</u></p> <ul style="list-style-type: none"> • Pyrimethamine 50–75 mg PO daily + leucovorin 10–25 mg PO daily (BIII), <i>or</i> • Ciprofloxacin 500 mg PO BID for 7 days (CI) as a second line alternative <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1600 mg) TIW (BIII) • Pyrimethamine 25 mg PO daily + leucovorin 5–10 mg PO daily (BIII) • Ciprofloxacin 500 mg TIW (CI) as a second-line alternative 	<p>Fluid and electrolyte management in patients with dehydration (AIII).</p> <p>Nutritional supplementation for malnourished patients (AIII).</p> <p>Immune reconstitution with ART may result in fewer relapses (AIII).</p>

Key to Acronyms: ACTG = AIDS Clinical Trials Group; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = ritonavir-boosted atazanavir; BID = twice a day; BIW = twice weekly; BOC = boceprevir; CD4 = CD4 T lymphocyte cell; CDC = The Centers for Disease Control and Prevention; CFU = colony-forming unit; CNS = central nervous system; CSF = cerebrospinal fluid; CYP3A4 = Cytochrome P450 3A4; ddl = didanosine; DOT = directly-observed therapy; DS = double strength; EFV = efavirenz; EMB = ethambutol; g = gram; G6PD = Glucose-6-phosphate dehydrogenase; GI = gastrointestinal; ICP = intracranial pressure; ICU = intensive care unit; IM = intramuscular; IND = investigational new drug; INH = isoniazid; IRIS = immune reconstitution inflammatory syndrome; IV = intravenous; LP = lumbar puncture; mg = milligram; mmHg = millimeters of mercury; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NSAID = non-steroidal anti-inflammatory drugs; PegIFN = Pegylated interferon; PI = protease inhibitor; PO = oral; PORN = Progressive Outer Retinal Necrosis; PZA = pyrazinamide; qAM = every morning; QID = four times a day; q(n)h = every “n” hours; qPM = every evening; RBV = ribavirin; RFB = rifabutin; RIF = rifampin; SQ = subcutaneous; SS = single strength; TID = three times daily, TIW = three times weekly; TVR = telaprevir; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

Evidence Rating:

Strength of Recommendation:

- A: Strong recommendation for the statement
- B: Moderate recommendation for the statement
- C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

- I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
- II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
- III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.

Table 3. Recommended Doses of First-Line Drugs for Treatment of Tuberculosis in Adults and Adolescents (Last updated May 7, 2013; last reviewed May 7, 2013)

Drug	Daily	3x/week
Isoniazid	5 mg/kg (usual dose 300 mg)	15 mg/kg (usual dose 900 mg)
Rifampin Note: Rifampin is not recommended in patients receiving HIV PIs, ETR, RPV, or EVG/COBI/TDF/FTC	10 mg/kg (usual dose 600 mg)	10 mg/kg (usual dose 600 mg)
Rifabutin without HIV PIs, EFV, RPV, or EVG/COBI/TDF/FTC	5 mg/kg (usual dose 300 mg)	5 mg/kg (usual dose 300 mg)
with HIV PIs	150 mg ^a	300 mg ^a
with EFV	450–600 mg	450–600 mg
with EVG/COBI/TDF/FTC	150 mg ^b	150 mg ^b
Pyrazinamide (weight-based dosing)		
40–55 kg	1000 mg (18.2–25.0 mg/kg)	1500 mg (27.3–37.5 mg/kg)
56–75 kg	1500 mg (20.0–26.8 mg/kg)	2500 mg (33.3–44.6 mg/kg)
76–90 kg	2000 mg (22.2–26.3 mg/kg)	3000 mg (33.3–39.5 mg/kg)
>90 kg	2000 mg ^c	3000 mg ^c
Ethambutol (weight-based dosing)		
40–55 kg	800 mg (14.5–20.0 mg/kg)	1200 mg (21.8–30.0 mg/kg)
56–75 kg	1200 mg (16.0–21.4 mg/kg)	2000 mg (26.7–35.7 mg/kg)
76–90 kg	1600 mg (17.8–21.1 mg/kg)	2400 mg (26.7–31.6 mg/kg)
>90 kg	1600 mg ^c	2400 mg ^c

^a Acquired rifamycin resistance has been reported in patients with inadequate rifabutin levels while on 150 mg twice weekly dosing together with ritonavir-boosted PIs. May consider therapeutic drug monitoring when rifabutin is used with a ritonavir-boosted PI and adjust dose accordingly.

^b Avoid co-administration of EVG/COBI/TDF/FTC with rifabutin, if possible. If used together, consider therapeutic drug monitoring and adjust dose accordingly.

^c Monitor for therapeutic response and consider therapeutic drug monitoring to assure dosage adequacy in patients who weigh >90 kg.

Key to Acronyms: COBI = cobicistat; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TDF = tenofovir disoproxil fumarate

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Prophylaxis in HIV-Infected Adults and Adolescents (page 1 of 3) (Last updated July 8, 2013; last reviewed July 8, 2013)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
<i>Pneumocystis</i> Pneumonia	CD4 count increased from <200 to >200 cells/μL for >3 months in response to ART (AI)	CD4 count <200 cells/mm ³ (AIII)	CD4 count increased from <200 cells/μL to >200 cells/μL for >3 months in response to ART (BII) If PCP was diagnosed when CD4 count was >200 cells/μL, continue prophylaxis for life regardless of CD4 count rise in response to ART (BIII) .	<ul style="list-style-type: none"> • CD4 count <200 cells/μL (AIII), <i>or</i> • If PCP recurred at CD4 count >200 cells/μL, prophylaxis should be continued for life (CIII).
<i>Toxoplasma gondii</i> Encephalitis	CD4 count increased to >200 cells/μL for >3 months in response to ART (AI)	CD4 count <100 to 200 cells/μL (AIII)	Successfully completed initial therapy, remain free of signs and symptoms of TE, and CD4 count >200 cells/μL for >6 months in response to ART (BI) .	CD4 count <200 cells/μL (AIII)
Microsporidiosis	Not applicable	Not applicable	No signs and symptoms of non-ocular (BIII) or ocular (CIII) microsporidiosis and CD4 count >200 cells/μL for >6 months in response to ART.	No recommendation
Disseminated <i>Mycobacterium avium</i> Complex Disease	CD4 count >100 cells/μL for ≥3 months in response to ART (AI)	CD4 count <50 cells/μL (AIII)	<p><u>If the following criteria are fulfilled (AI):</u></p> <ul style="list-style-type: none"> • Completed ≥12 months of therapy, <i>and</i> • No signs and symptoms of MAC disease, <i>and</i> • Have sustained (>6 months) CD4 count >100 cells/μL in response to ART. 	CD4 count <100 cells/μL (AIII)
Salmonellosis	Not applicable	Not applicable	Resolution of <i>Salmonella</i> infection and after response to ART with sustained viral suppression and CD4 counts >200 cells/μL (CII)	No recommendation
Bartonellosis	Not applicable	Not applicable	<ul style="list-style-type: none"> • Received at least 3–4 months of treatment, <i>and</i> • CD4 count >200 cells/μL for ≥6 months (CIII) • Some specialists would only discontinue therapy if <i>Bartonella</i> titers have also decreased by four-fold (CIII). 	No recommendation
Mucosal Candidiasis	Not applicable	Not applicable	If used, reasonable to discontinue when CD4 count >200 cells/μL (AIII) .	No recommendation

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Prophylaxis in HIV-Infected Adults and Adolescents (page 2 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Cryptococcal Meningitis	Not applicable	Not applicable	<p><u>If the following criteria are fulfilled (BII):</u></p> <ul style="list-style-type: none"> Completed initial (induction and consolidation) therapy, <i>and</i> Received at least 1 year of maintenance therapy, <i>and</i> Remain asymptomatic of cryptococcal infection, <i>and</i> CD4 count ≥ 100 cells/μL for >3 months, and with suppressed plasma HIV RNA in response to ART 	CD4 count <100 cells/ μ L (AIII)
<i>Histoplasma capsulatum</i> Infection	CD4 count >150 cells/ μ L for 6 months while on ART (BIII)	For patients at high risk of acquiring histoplasmosis, restart at CD4 count <150 cells/ μ L (CIII)	<p><u>If the following criteria (AI) are fulfilled:</u></p> <ul style="list-style-type: none"> Received itraconazole for >1 year, <i>and</i> Negative fungal blood cultures, <i>and</i> CD4 count ≥ 150 cells/μL for ≥ 6 months in response to ART, <i>and</i> Serum <i>Histoplasma antigen</i> <2 ng/mL 	CD4 count <150 cells/ mm^3 (BIII)
Coccidioidomycosis	CD4 count ≥ 250 cells/ μ L for ≥ 6 months (CIII)	Restart at CD4 count <250 cells/ μ L (BIII)	<p><u>Only for patients with focal coccidioidal pneumonia (AII):</u></p> <ul style="list-style-type: none"> Clinically responded to ≥ 12 months antifungal therapy, with CD4 count >250 cells/mm^3, and receiving effective ART. Should continue monitoring for recurrence with serial chest radiographs and coccidioidal serology. <p><u>For patients with diffuse pulmonary (BIII), disseminated non-meningeal (BIII), or meningeal diseases (AII):</u></p> <ul style="list-style-type: none"> Suppressive therapy should be continued indefinitely, even with increase in CD4 count on ART. 	No recommendation

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Prophylaxis in HIV-Infected Adults and Adolescents (page 3 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Cytomegalovirus Retinitis	Not applicable	Not applicable	<ul style="list-style-type: none"> • CMV treatment for >3 to 6 months; and with CD4 count >100 cells/μL for >3 to 6 months in response to ART (AII) • Therapy should be discontinued only after consultation with an ophthalmologist, taking into account anatomic location of lesions, vision in the contralateral eye, and feasibility of regular ophthalmologic monitoring. • Routine (i.e., every 3 months) ophthalmologic follow-up is recommended for early detection of relapse or immune restoration uveitis, and then annually after immune reconstitution (AIII). 	CD4 count <100 cells/μL (AIII)
<i>Penicillium marneffei</i> Infection	CD4 count >100 cells/μL for >6 months in response to ART (BII)	CD4 count <100 cells/μL (BIII)	CD4 count >100 cells/μL for ≥6 months in response to ART (BII)	<ul style="list-style-type: none"> • CD4 count <100 cells/μL (AIII), or • If penicilliosis recurs at CD4 count >100 cells/μL (CIII)
Visceral Leishmaniasis (and possibly cutaneous leishmaniasis in immunocompromised patients with multiple relapses)	Not applicable	Not applicable	There is no consensus regarding when to stop secondary prophylaxis. Some investigators suggest that therapy can be stopped if CD4 count increases to >200 to 350 cells/μL for 3–6 months in response to ART, but others suggest that therapy should be continued indefinitely.	No recommendation
<i>Isospora belli</i> Infection	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/μL for >6 months in response to ART and without evidence of <i>I. belli</i> infection (BIII)	No recommendation

Key to Acronyms: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte cell; CMV = cytomegalovirus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis pneumonia*; TE = *Toxoplasma encephalitis*

Evidence Rating:

Strength of Recommendation:

- A: Strong recommendation for the statement
- B: Moderate recommendation for the statement
- C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

- I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
- II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
- III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 1 of 14) (Last updated May 7, 2013; last reviewed May 7, 2013)

This table provides clinicians with information regarding known or suspected pharmacokinetic interactions between drugs commonly used for treatment or prevention of HIV-associated opportunistic infections or for treatment of HIV infection. Note that there may be substantial inter-patient variability in the magnitude of the interactions. Moreover, the table only provides suspected interactions between 2 drugs when used in combination, but cannot be used to predict the interaction potential when three or more drugs with similar metabolic pathways are co-administered. In these cases, alternative options with less drug interaction potential or therapeutic drug monitoring (if available), should be considered.

Throughout the table, two recommendations are commonly used when concomitant administration of two drugs may lead to untoward consequences. The definitions for these terms used in the Recommendations column are summarized below:

Co-administration should be avoided.

Indicates there is strong evidence or likelihood that the drug-drug interaction will result in either

- 1) Markedly decreased concentrations of one or both drugs, which may render one or both drugs ineffective, or
- 2) Increased concentrations of one or both drugs, which may result in excessive risk of toxicity that cannot be managed with a dose modification of one or both drugs.

Co-administration should be avoided if possible.

There is a potential for significant pharmacokinetic interactions. However, co-administration of the drugs may be necessary if there are no other reasonable options that provide a more favorable risk-benefit assessment. In some instances, a suggested strategy is provided with the recommendation based upon available knowledge and alternatives. If other more favorable options exist, the clinician is advised to consider changing components of the regimen to accommodate a more effective and/or safer regimen.

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Artemether-Lumefantrine	Darunavir/ritonavir	Artemether AUC ↓ 16%; DHA AUC ↓ 18%; lumefantrine AUC ↑ 2.5-fold	Clinical significance unknown. Monitor for anti-malarial efficacy and lumefantrine toxicities.
	Efavirenz	Artemether AUC ↓ 79%; DHA AUC ↓ 75%; lumefantrine AUC ↓ 56%	Clinical significance unknown. If used, monitor closely for anti-malarial efficacy.
	Etravirine	Artemether AUC ↓ 38%; DHA AUC ↓ 15%; lumefantrine AUC ↓ 13%	Clinical significance unknown. If used, monitor closely for anti-malarial efficacy.
	Lopinavir/ritonavir	Artemether AUC ↓ 40%; DHA AUC ↓ 17%; lumefantrine AUC ↑ 470%	Data based on single dose study. Clinical significance unknown. Monitor for anti-malarial efficacy and lumefantrine toxicities.
	Nevirapine	Artemether AUC ↓ 72%; DHA AUC ↓ 37%; lumefantrine (no difference in one study, but AUC ↑ 55.6% in another study)	Clinical significance unknown. Monitor for anti-malarial efficacy.
	Rifampin	Artemether AUC ↓ 89%; DHA AUC ↓ 85%; lumefantrine AUC ↓ 68%	Co-administration should be avoided.
Atovaquone	Atazanavir/ritonavir	Atovaquone AUC ↓ 46%; no data with unboosted atazanavir (based on a single-dose PK study using atovaquone 250 mg/proguanil 100 mg fixed-dose combination tablet; no interaction data between boosted or unboosted atazanavir and atovaquone suspension)	Dose adjustment not established; if co-administered, monitor for decreased atovaquone efficacy.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 2 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Atovaquone, continued	Doxycycline	Atovaquone concentrations ↓ 40% with tetracycline; interaction study with doxycycline not available	Dose adjustment not established; if co-administered, monitor for decreased atovaquone efficacy.
	Efavirenz	Atovaquone AUC ↓ 75% (based on a single-dose PK study using atovaquone 250 mg/proguanil 100 mg fixed-dose combination tablet; no interaction data between efavirenz and atovaquone suspension)	Co-administration should be avoided if possible. If co-administered, monitor for decreased atovaquone efficacy.
	Lopinavir/ritonavir	Atovaquone AUC ↓ 74% (based on a single-dose PK study using atovaquone 250 mg/proguanil 100 mg fixed-dose combination tablet; no interaction data between lopinavir/ritonavir and atovaquone suspension)	Co-administration should be avoided if possible. If co-administered, monitor for decreased atovaquone efficacy.
	Rifabutin	Atovaquone AUC ↓ 34%; rifabutin AUC ↓ 19%	Dose adjustment not established; if co-administered, monitor for decreased atovaquone efficacy.
	Rifampin	Atovaquone concentrations ↓ 52%; rifampin concentrations ↑ 37%	Co-administration should be avoided.
	Zidovudine	Zidovudine AUC ↑ 31%	No dose adjustment necessary; monitor for zidovudine-associated toxicities.
Boceprevir	Atazanavir/ritonavir	Boceprevir AUC no change; atazanavir AUC ↓ 35%, C _{min} ↓ 49%; ritonavir AUC ↓ 36%	Co-administration should be avoided.
	Clarithromycin	May ↑ concentrations of clarithromycin	No dose adjustment necessary in patients with normal renal function. To avoid drug interaction, consider switching to azithromycin.
	Darunavir/ritonavir	Boceprevir AUC ↓ 32%, C _{min} ↓ 35%; darunavir AUC ↓ 44%, C _{min} ↓ 59%; ritonavir AUC ↓ 27%	Co-administration should be avoided.
	Efavirenz	Boceprevir AUC ↓ 19%, C _{min} ↓ 44%; efavirenz AUC ↑ 20%	Significance unknown; co-administration should be avoided.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	No PK data, bi-directional interaction possible	Co-administration should be avoided.
	Etravirine	Boceprevir AUC ↑ 10%, C _{min} ↓ 12%; etravirine AUC ↓ 23%, C _{min} ↓ 29%	Clinical significance of this interaction is unknown.
	Itraconazole, ketoconazole, posaconazole, voriconazole	Boceprevir AUC ↑ 230% when co-administered with ketoconazole 400 mg bid. Concentrations of azoles may be ↑	Doses of ketoconazole and itraconazole should not exceed 200 mg/day. Consider monitoring azole drug concentrations and adjust dose accordingly. Monitor for boceprevir-associated toxicities.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 3 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Boceprevir, continued	Lopinavir/ritonavir	Boceprevir AUC ↓ 45%, C _{min} ↓ 57%; lopinavir AUC ↓ 34%, C _{min} ↓ 43%; ritonavir AUC ↓ 22%	Co-administration should be avoided.
	Raltegravir	No significant interaction.	This combination can be co-administered without dosage adjustment
	Rifabutin	↑ in rifabutin concentrations are anticipated, while exposure of boceprevir may be ↓	Co-administration should be avoided, if possible. If used in combination, consider monitoring rifabutin concentration and adjust dose accordingly.
	Rifampin	No PK data. Significant ↓ in boceprevir exposure is anticipated.	Co-administration should be avoided.
Caspofungin	Efavirenz, nevirapine	Possible ↓ in caspofungin concentrations based on regression analyses of patient PK data. No formal PK study available.	Manufacturer recommends consider increasing maintenance dose of caspofungin to 70 mg/day when co-administered with CYP450 inducers.
	Rifampin	Caspofungin C _{min} ↓ 30%	Caspofungin dose should be increased to 70 mg/day.
Clarithromycin	Atazanavir	Atazanavir C _{min} ↑ 91%, AUC ↑ 28%; clarithromycin AUC ↑ 94%, C _{min} ↑ 160% Co-administration with atazanavir/ritonavir has not been studied.	Because of concerns for QTc prolongation when these drugs are used in combination, reduce clarithromycin dose by 50% or switch to azithromycin.
	Boceprevir	Concentrations of clarithromycin may be ↑	No dose adjustment in patients with normal renal function. To avoid drug interaction, consider switching to azithromycin.
	Darunavir/ritonavir	Clarithromycin AUC ↑ 57%, C _{min} ↑ 174%	No dose adjustment in patients with normal renal function. To avoid drug interaction, consider switching to azithromycin.
	Efavirenz	Clarithromycin AUC ↓ 39%	Significance unknown; consider switching to azithromycin.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Clarithromycin, cobicistat, and elvitegravir concentrations may be increased.	CrCl > 60 mL/min: no dosage adjustment. CrCl 50–60 mL/min: reduce clarithromycin dose by 50%. To avoid drug interaction, consider switching to azithromycin.
	Etravirine	Clarithromycin AUC ↓ 39%; etravirine C _{min} ↑ 46%, AUC ↑ 42%	Significance unknown; consider switching to azithromycin.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 4 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Clarithromycin, continued	Fluconazole	Clarithromycin AUC ↑ 18%, C _{min} ↑ 33%	No dose adjustment necessary in patients with normal renal function.
	Itraconazole	Possible bi-directional CYP3A4 inhibition and increased exposure of both drugs.	Monitor for toxicities of both itraconazole and clarithromycin, consider monitoring drug concentrations and adjust dose accordingly, or consider switching to azithromycin.
	Lopinavir/ritonavir	Increased clarithromycin exposure expected.	No dose adjustment necessary in patients with normal renal function. To avoid drug interaction, consider switching to azithromycin.
	Maraviroc	Potential for inhibition of maraviroc metabolism and ↑ maraviroc concentration.	Decrease maraviroc dose to 150 mg BID or switch to azithromycin.
	Nevirapine	Clarithromycin AUC ↓ 29%, C _{min} ↓ 46%	Co-administration should be avoided if possible; consider switching to azithromycin.
	Rifabutin	Clarithromycin AUC ↓ by 44%; rifabutin AUC ↑ 76%–99%.	Consider reducing rifabutin dose, monitor for rifabutin-associated toxicities, Consider monitoring serum concentration and adjust dose accordingly; or switch to azithromycin.
	Rifampin	Mean clarithromycin concentration ↓ 87%	This combination should be avoided. Switch to azithromycin.
	Saquinavir	Saquinavir C _{max} ↑ 187%, AUC ↑ 177%; clarithromycin C _{max} and AUC ↑ 40% (studied with saquinavir 1200 mg TID) Clarithromycin has not been studied with ritonavir-boosted saquinavir.	No dose adjustment necessary in patients with normal renal function. Clarithromycin dose adjustment may be necessary in patients with renal dysfunction. Monitor closely because of additive risk of QTc prolongation associated with increased concentrations of both drugs. Consider switching to azithromycin.
	Telaprevir	Concentrations of both telaprevir and clarithromycin may be increased during co-administration.	Use with caution and monitor for adverse events, including QT prolongation. Reduce clarithromycin dose during concomitant use with telaprevir in patients with impaired renal function. Consider switching to azithromycin.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 5 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Clarithromycin, continued	Tipranavir/ritonavir	Clarithromycin AUC ↑ 19%, C _{min} ↑ 68%; tipranavir AUC ↑ 66%, C _{min} ↑ 100%	Monitor for tipranavir-associated toxicities. No dose adjustment necessary in patients with normal renal function. Clarithromycin dose adjustment may be necessary in patients with renal dysfunction. Consider switching to azithromycin.
Dapsone	Rifampin	Dapsone concentrations ↓ 7 to 10-fold and half-life (t _{1/2}) ↓ from 24 to 11 hours.	Co-administration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
Doxycycline	Atovaquone	Atovaquone concentrations ↓ by approximately 40% with tetracycline; interaction study with doxycycline not available.	Until doxycycline-atovaquone interaction data become available, avoid this combination if possible.
	Rifampin	Doxycycline AUC ↓ by 59%	Potential for decreased doxycycline efficacy; monitor closely for therapeutic failure.
Erythromycin	Itraconazole	Itraconazole C _{max} ↑ 44%, AUC ↑ 36%. Potential for ↑ in erythromycin concentration.	Monitor for toxicities of both drugs, potential for QT prolongation; monitor itraconazole concentrations and adjust dose accordingly, or consider alternative azole or macrolide.
	Telaprevir	Concentrations of telaprevir and erythromycin may ↑ during co-administration.	Use with caution and monitor for adverse events, including QT prolongation.
Fluconazole	Clarithromycin	Clarithromycin AUC ↑ 18%, C _{min} ↑ 33%	No dose adjustment necessary in patients with normal renal function.
	Efavirenz	Efavirenz AUC ↑ 16%; no change in fluconazole AUC.	No dose adjustment necessary.
	Etravirine	Etravirine AUC ↑ 86%, C _{min} ↑ 109%	Co-administer with caution. Monitor for etravirine-associated toxicities.
	Nevirapine	Nevirapine concentrations ↑ 100% (compared with historic control).	Co-administration should be avoided, if possible. If co-administered, monitor for nevirapine-associated toxicities.
	Rifabutin	Rifabutin AUC ↑ 80%; no effect on fluconazole exposure.	Monitor for rifabutin-associated toxicities; consider monitoring rifabutin concentrations; may need to reduce rifabutin dose to 150 mg/day.
	Rifampin	Fluconazole AUC ↓ 23%–56%; no change in rifampin exposure.	Monitor for antifungal efficacy; may need to increase fluconazole dose.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 6 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Fluconazole, continued	Saquinavir	Saquinavir C_{max} ↑ 56%, AUC ↑ 50% (studied with saquinavir 1200 mg TID). Fluconazole has not been studied with ritonavir-boosted saquinavir.	Significance unknown. No dosage adjustment needed.
	Tipranavir/ritonavir	Tipranavir AUC ↑ 50%, C_{min} ↑ 69%	Monitor for tipranavir-associated toxicities; fluconazole doses >200 mg/day not recommended.
	Zidovudine	Fluconazole ↓ glucuronidation of zidovudine; fluconazole 400 mg/day results in zidovudine AUC ↑ 74%	Monitor for zidovudine-associated toxicities.
Itraconazole	Boceprevir	Concentrations of itraconazole and/or boceprevir may be ↑	Itraconazole dose should not exceed 200 mg/day. Monitor itraconazole concentration and adjust dose accordingly.
	Clarithromycin	Possible bi-directional CYP3A4 inhibition and ↑ exposure of both drugs.	Monitor for toxicities of both itraconazole and clarithromycin. Monitor itraconazole concentration and adjust dose accordingly. Alternatively, consider switching to azithromycin.
	Efavirenz	Itraconazole AUC ↓ 39%, C_{min} ↓ 44% in PK studies; No change to efavirenz AUC. Failure to achieve therapeutic itraconazole concentrations has been reported.	Co-administration should be avoided if possible. If used in combination, monitor itraconazole concentrations and adjust dose accordingly.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Cobicistat, elvitegravir, and itraconazole serum concentration may be ↑	Avoid itraconazole >200 mg/day. Monitor itraconazole serum concentrations with co-administration.
	Erythromycin	Potential for bi-directional inhibition of metabolism and ↑ serum concentrations of both drugs.	Monitor for toxicities of both drugs, potential for QT prolongation; monitor itraconazole concentrations and adjust dose accordingly, or consider alternative azole or macrolide.
	Etravirine	Etravirine concentration may be ↑; Itraconazole concentration may be ↓. Extent of the interaction unknown.	Dose adjustment with itraconazole may be necessary depending on the presence of other concomitant ARV drugs (e.g., PIs). Monitor itraconazole concentrations and adjust dose accordingly.
	Maraviroc	Potential for inhibition of maraviroc metabolism and ↑ in maraviroc concentration.	Decrease maraviroc dose to 150 mg twice daily.
	Micafungin	Itraconazole AUC ↑ 22%	No dose adjustment necessary.
	Nevirapine	Itraconazole C_{max} ↓ 38%, AUC ↓ 61%; nevirapine: no change	Monitor itraconazole concentrations and adjust accordingly dose; monitor therapeutic efficacy.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 7 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Itraconazole, continued	PIs	Potential for bi-directional CYP3A4 inhibition with ↑ exposure of both drugs.	Monitor for PI-associated toxicities; monitor itraconazole concentrations and itraconazole-associated toxicities
	Rifabutin	Itraconazole AUC ↓ 70%; potential for inhibition of rifabutin metabolism and ↑ rifabutin exposure.	Co-administration should be avoided, if possible. If the combination is to be used, monitor itraconazole concentrations and adjust dose accordingly; monitor for rifabutin-associated toxicities and consider monitoring rifabutin concentrations.
	Rifampin	Itraconazole AUC ↓ 64%–88%; no change in rifampin concentrations.	Co-administration should be avoided. Consider alternative antifungal and/or antimycobacterial agent(s).
	Rilpivirine	Potential ↑ in rilpivirine exposure or ↓ in itraconazole.	No dose adjustment for rilpivirine; monitor for rilpivirine-associated toxicities. Consider monitoring itraconazole concentration and adjust dose as necessary.
	Telaprevir	Concentrations of itraconazole and telaprevir may be ↑	If co-administration is necessary, high doses of itraconazole (>200 mg/day) are not recommended. Monitor for toxicities to both drugs. Consider monitoring itraconazole concentration and adjust dose accordingly.
Mefloquine	Rifampin	Mefloquine AUC ↓ 68%.	Co-administration should be avoided, if possible. Use alternative anti-malarial drug or rifabutin.
	Ritonavir	When studied with ritonavir 200 mg twice daily—ritonavir AUC ↓ 31%, C _{min} ↓ 43%; no substantial change in mefloquine PK. Effect on exposure of ritonavir-boosted PIs unknown.	Use mefloquine with caution with PIs.
Micafungin	Itraconazole	Itraconazole AUC ↑ 22%	No dose adjustment necessary.
Posaconazole	Atazanavir (+/- ritonavir)	With unboosted-atazanavir—atazanavir AUC ↑ 268%; with ritonavir-boosted atazanavir—atazanavir AUC ↑ 146%	Co-administration should be avoided, if possible; or monitor atazanavir concentrations and adjust doses accordingly; monitor for atazanavir-associated toxicities.
	Boceprevir	Posaconazole concentration may be ↑	Use with caution, considering monitoring posaconazole concentration and adjust dose accordingly.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 8 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Posaconazole, continued	Efavirenz	Posaconazole AUC ↓ 50%, C _{max} ↓ 45%	Co-administration should be avoided, if possible; or monitor posaconazole concentrations and adjust doses accordingly.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Cobicistat, elvitegravir, and posaconazole concentrations may be ↑	Monitor posaconazole concentration and adjust dose accordingly.
	Etravirine	Etravirine exposure may be ↑; posaconazole exposure unlikely to be affected.	No dose adjustment necessary; monitor for etravirine-associated toxicities.
	Fosamprenavir	Amprenavir AUC ↓ 65%; posaconazole AUC ↓ 23% (studied without ritonavir boosting). No data for fosamprenavir/ritonavir.	Co-administration should be avoided, or monitor drug concentrations and adjust doses accordingly.
	Rifabutin	Posaconazole AUC ↓ 49%; rifabutin AUC ↑ 72%.	Co-administration should be avoided, if possible, or monitor posaconazole and rifabutin concentrations and adjust doses accordingly; monitor clinical response.
	Rifampin	Posaconazole exposure may be ↓ significantly.	Co-administration should be avoided, if possible. If used, monitor posaconazole concentrations and adjust dose accordingly.
	Rilpivirine	Potential ↑ in rilpivirine concentrations.	Monitor for rilpivirine-associated toxicities.
	Ritonavir	Ritonavir AUC ↑ 80%, C _{max} ↑ 49%	No ritonavir dose adjustment necessary.
	Telaprevir	Concentrations of posaconazole and telaprevir may be ↑	Use with caution with increased monitoring for posaconazole- or telaprevir-associated toxicities, including QT prolongation. Consider monitoring posaconazole level and adjust dose accordingly.
Proguanil	Atazanavir/ritonavir	Proguanil AUC ↓ 41%; no data with unboosted atazanavir.	Use with caution.
	Efavirenz	Proguanil AUC ↓ 43%	Use with caution.
	Lopinavir/ritonavir	Proguanil AUC ↓ 38%	Use with caution.
Ribavirin	Didanosine	↑ intracellular concentrations of ddA-TP	↑ serious didanosine-associated mitochondrial toxicities. Co-administration should be avoided.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 9 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifabutin	Atovaquone	Atovaquone AUC ↓ 34%; rifabutin AUC ↓ 19%.	Co-administration should be avoided. If used, monitor for therapeutic response.
	Boceprevir	↑ in rifabutin concentrations are anticipated, while exposure of boceprevir may be ↓	Co-administration should be avoided, if possible. If used in combination, consider monitoring rifabutin concentration and adjust dose accordingly.
	Clarithromycin	Clarithromycin AUC ↓ 44%; rifabutin AUC ↑ 76%–99%.	Consider reducing rifabutin dose, monitor for rifabutin-associated toxicities, Consider monitoring serum concentration and adjust dose accordingly; or switch to azithromycin.
	Efavirenz	Rifabutin AUC ↓ 38%; no change in efavirenz exposure.	Increase rifabutin dose to 450–600 mg/day; effect of efavirenz + PI(s) on rifabutin concentrations has not been studied.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Elvitegravir AUC ↓ 21%, C _{min} ↓ 67%; rifabutin active metabolite (25-O-desacetyl rifabutin) AUC ↑ 625%	Co-administration should be avoided, if possible. Consider using alternative antimycobacterial agent or alternative ARV drug. If used, consider rifabutin 150 mg once daily or every other day, consider monitoring rifabutin concentrations and adjust dose accordingly.
	Etravirine	Etravirine C _{min} ↓ 35% and AUC ↓ 37%; rifabutin AUC ↓ 17%.	Use standard rifabutin dose of 300 mg daily if not used with a ritonavir-boosted PI. In patients receiving a ritonavir-boosted PI, consider alternative agents if possible, or use serum concentration to guide dosing of rifabutin.
	Fluconazole	Rifabutin AUC ↑ 80%; no effect on fluconazole exposure.	Monitor for rifabutin toxicity and consider monitoring rifabutin concentrations and adjust dose accordingly; may need to reduce rifabutin dose to 150 mg/day.
	Itraconazole	Itraconazole AUC ↓ 70%; potential for ↑ rifabutin exposure.	Co-administration should be avoided, if possible. If the combination is to be used, monitor itraconazole and rifabutin concentrations and adjust doses accordingly. Monitor for rifabutin-associated toxicities.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 10 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifabutin, continued	Maraviroc	Concentration of maraviroc may be ↓	If used without another strong CYP3A4 inducer or inhibitor, maraviroc 300 mg BID. If used with a strong CYP3A4 inhibitor, use maraviroc 150 mg BID.
	Nevirapine	Rifabutin AUC ↑ 17%, 25-O-desacetyl rifabutin AUC ↑ 24%; nevirapine C _{min} ↓ 16%.	No dose adjustment necessary.
	PI boosted by ritonavir	Significant ↑ in rifabutin concentrations.	Use rifabutin 150 mg daily or 300 mg 3 times/week. Consider monitoring rifabutin concentrations and adjust dose accordingly.
	Posaconazole	Posaconazole AUC ↓ 49%; rifabutin AUC ↑ 72%.	Co-administration should be avoided, if possible, or monitor posaconazole and rifabutin concentrations and adjust doses accordingly; monitor clinical response.
	Rilpivirine	Rilpivirine AUC ↓ 46%	Co-administration should be avoided.
	Telaprevir	Concentrations of telaprevir may be ↓, while rifabutin concentrations may be ↑	Co-administration should be avoided.
	Voriconazole	Voriconazole AUC ↓ 79%; rifabutin AUC ↑ 3-fold.	Co-administration should be avoided, if possible. If used in combination, monitor voriconazole and rifabutin concentrations and adjust dose accordingly. Monitor for clinical responses and toxicities.
Rifampin	Artemether/lumefantrine	Artemether AUC ↓ 89%; DHA AUC ↓ 85%; lumefantrine AUC ↓ 68%	Co-administration should be avoided.
	Atovaquone	Atovaquone concentrations ↓ 52%; rifampin concentrations ↑ 37%	Co-administration should be avoided.
	Boceprevir	No PK data. Significant ↓ in boceprevir exposure is anticipated.	Co-administration should be avoided.
	Caspofungin	Caspofungin C _{min} ↓ 30%	Caspofungin dose should be increased to 70 mg/day.
	Clarithromycin	Mean clarithromycin concentrations ↓ 87%	This combination should be avoided; consider switching to azithromycin.
	Dapsone	Dapsone concentrations ↓ 7- to 10-fold and half-life (t _{1/2}) ↓ from 24 to 11 hours.	Co-administration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
	Doxycycline	Doxycycline AUC ↓ by 59%	Potential for decreased doxycycline efficacy; monitor closely for therapeutic failure.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 11 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifampin, continued	Efavirenz	Efavirenz AUC ↓ 22%, C _{min} ↓ 25%; no change in rifampin exposure.	Maintain efavirenz dose at 600 mg once daily and monitor for virologic response. Some clinicians suggest increasing efavirenz dose to 800 mg per day in patients >60 kg.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Cobicistat and elvitegravir concentrations may be significantly ↓	Co-administration should be avoided. Consider an alternative antimycobacterial agent or alternative antiretroviral drug regimen.
	Etravirine	Potential significant ↓ in etravirine concentration.	Co-administration should be avoided.
	Fluconazole	Fluconazole AUC ↓ by 23%–56%; no change in rifampin exposure.	Monitor for antifungal efficacy, may need to increase fluconazole dose.
	Itraconazole	Itraconazole AUC ↓ 64%–88%; no change in rifampin concentrations.	Co-administration should be avoided. Consider alternative antifungal and/or antimycobacterial agent(s).
	Maraviroc	Maraviroc AUC ↓ 63%, C _{min} decreased 67%	Increase maraviroc dose to 600 mg twice daily or use alternative antimycobacterial agent.
	Nevirapine	Nevirapine AUC ↓ by >50%, C _{min} ↓ 21–37%; no change in rifampin concentrations.	This combination should be avoided if possible. If adding nevirapine to rifampin is necessary, initiate nevirapine at 200 mg twice daily (i.e., no lead-in period). Do not use nevirapine extended-release formulation.
	Posaconazole	Posaconazole concentrations may be ↓ significantly.	Co-administration should be avoided if possible. If used, monitor posaconazole concentrations and adjust dose if necessary.
	PI (+/- ritonavir-boosting)	Significantly ↓ PI exposure (>75%) despite ritonavir boosting	Co-administration should be avoided.
	Raltegravir	Raltegravir AUC ↓ 40%, C _{min} ↓ 60%	Increase raltegravir dose to 800 mg PO twice daily, monitor for antiretroviral efficacy, or switch to rifabutin.
	Rilpivirine	Rilpivirine AUC ↓ 80%	Co-administration should be avoided.
	Telaprevir	Telaprevir AUC ↓ 92%	Co-administration should be avoided.
	Voriconazole	Voriconazole AUC ↓ 96%	Co-administration should be avoided.
	Zidovudine	Zidovudine AUC ↓ 48%	Monitor for zidovudine efficacy.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 12 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Telaprevir	Atazanavir/ritonavir	Telaprevir AUC ↓ 20%, C _{min} ↓ 15%; atazanavir C _{min} ↑ 85%	No dosage adjustment necessary.
	Clarithromycin	Concentrations of telaprevir and clarithromycin may be ↑ during co-administration.	Use with caution and monitor for adverse events, including QT prolongation. Reduce clarithromycin dose during concomitant use with telaprevir in patients with impaired renal function. Consider switching to azithromycin.
	Darunavir/ritonavir	Telaprevir AUC ↓ 35%, C _{min} ↓ 32%; darunavir AUC and C _{min} ↓ 40%.	Co-administration should be avoided.
	Efavirenz	Telaprevir AUC ↓ 26%; C _{min} ↓ 47%	Increase telaprevir dose to 1125 mg every 8 hours.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	No data. Potential for bi-directional interactions.	Co-administration should be avoided.
	Erythromycin	Concentrations of telaprevir and erythromycin may be ↑ during co-administration.	Use with caution and monitor for adverse events, including QT prolongation.
	Fosamprenavir/ritonavir	Telaprevir AUC ↓ 32%, C _{min} ↓ 30%; amprenavir AUC ↓ 47%, C _{min} ↓ 56%	Co-administration should be avoided.
	Itraconazole	Concentrations of itraconazole and telaprevir may be ↑	If co-administration is necessary, high doses of itraconazole (>200 mg/day) are not recommended. Monitor for toxicities to both drugs. Consider monitoring itraconazole concentration and adjust dose accordingly.
	Lopinavir/ritonavir	Telaprevir AUC ↓ 54%, C _{min} ↓ 52%	Co-administration should be avoided.
	Posaconazole	Concentrations of posaconazole and telaprevir may be ↑	Use with caution and monitor for posaconazole-associated toxicities, including QT prolongation. Consider monitoring posaconazole concentration and adjust dose accordingly.
	Rifabutin	Concentrations of telaprevir may be ↑, while rifabutin concentrations may be ↑	Co-administration should be avoided
	Rifampin	Telaprevir AUC ↓ 92%	Co-administration should be avoided
	Tenofovir	Tenofovir C _{max} , AUC, and C _{min} ↑ 30%–41%	Monitor for tenofovir-associated toxicities.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 13 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Telaprevir , continued	Voriconazole	Potential interaction; magnitude and direction unknown.	Co-administration should be avoided unless benefit is considered to outweigh risks; monitor for voriconazole-associated toxicities, including QT prolongation. Consider monitoring voriconazole concentration and adjust dose accordingly.
Tenofovir	Acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir	Potential for competitive active tubular secretion with these antiviral drugs.	Monitor for efficacy and toxicities of the antiviral agents and tenofovir.
	Atazanavir	Atazanavir AUC ↓ 25%, C _{min} ↓ 40%; tenofovir AUC ↑ 24%.	Atazanavir dose should be 300 mg daily given with ritonavir 100 mg daily when co-administered with tenofovir; monitor for tenofovir-associated toxicities.
	Darunavir/ritonavir	Tenofovir AUC ↑ 22%, C _{min} ↑ 37%	Monitor for tenofovir-associated toxicities.
	Didanosine	Didanosine AUC and C _{max} ↑ 48%–60%	Co-administration should be avoided. If co-administered, didanosine dose should be decreased to 250 mg once daily.
	Lopinavir/ritonavir	Tenofovir AUC ↑ 34%	Monitor for tenofovir-associated toxicities.
	Telaprevir	Tenofovir C _{max} , AUC and C _{min} ↑ 30–41%	Monitor for tenofovir-associated toxicities.
Voriconazole	Boceprevir	Concentrations of voriconazole may be ↑	Use with caution. Consider monitoring voriconazole concentration and adjust dose accordingly.
	Efavirenz	Voriconazole C _{max} ↓ 36–61%, AUC ↓ 55–77%; efavirenz C _{max} ↑ 38%, AUC ↑ 44%	Increase voriconazole maintenance dose to 400 mg q12h and decrease efavirenz to 300 mg daily. Consider monitoring voriconazole and/or efavirenz concentration and adjust doses accordingly.
	Elvitegravir/cobicistat/tenofovir/emtricitabine	Voriconazole, elvitegravir, and cobicistat concentrations may be ↑	Monitor for voriconazole-associated toxicities. Consider monitoring voriconazole concentration and adjust dose accordingly.
	Etravirine	Voriconazole AUC ↑ 14%, C _{min} ↑ 23%; etravirine AUC ↑ 36%, C _{min} ↑ 52%	No dose adjustment necessary; monitor for etravirine-associated toxicities. Consider monitoring voriconazole concentration and adjust dose accordingly.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 14 of 14)

Drug	Interacting With	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Voriconazole, continued	Nevirapine	Potential for ↓ voriconazole concentrations; however, no formal interaction data are available.	Monitor for therapeutic efficacy of voriconazole; consider monitoring voriconazole concentrations and adjust dose accordingly.
	PI boosted with ritonavir	Voriconazole AUC ↓ 39% (studied with ritonavir 100 mg BID). No interaction data for individual boosted PIs; however, potential for ↑ PI concentrations and ↓ voriconazole concentrations.	Consider monitoring voriconazole concentrations and adjust dose accordingly; monitor for PI-associated toxicities.
	Rifabutin	Voriconazole AUC ↓ 79%; rifabutin AUC ↑ 3-fold.	Co-administration should be avoided, if possible; if used in combination, monitor voriconazole and rifabutin concentrations, clinical responses, and toxicities from both drugs.
	Rifampin	Voriconazole AUC ↓ 96%	Co-administration should be avoided.
	Rilpivirine	No PK data. Possible ↑ rilpivirine concentration	Monitor efficacies and toxicities of both drugs. Consider monitoring voriconazole concentration and adjust dose accordingly.
	Telaprevir	Potential interaction; magnitude and direction unknown.	Co-administration should be avoided unless benefit is considered to outweigh risks; monitor for voriconazole-associated toxicities, including QT prolongation. Consider monitoring voriconazole concentration and adjust dose accordingly.

Key to Acronyms: ARV = antiretroviral; AUC = area under the curve; BID = twice daily = C_{max} = maximum concentration; C_{min} = minimum concentration; CrCl = creatinine clearance; CYP3A4 = Cytochrome P450 3A4; ddA-TP = dideoxyadenosine triphosphate; DHA = dihydroartemisinin; PI = protease inhibitor; PK = pharmacokinetic; TID = three times a day

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 1 of 5) (Last updated May 7, 2013; last reviewed May 7, 2013)

Drugs	Common or Serious Adverse Reactions
Acyclovir	Generally well-tolerated. Crystalluria (with high dose or pre-existing renal impairment), neurotoxicity (high doses, especially in patients with renal impairment; agitation, confusion, hallucination, seizure, coma), nephrotoxicity secondary to obstructive urolithiasis (particularly after rapid IV infusion), thrombophlebitis at peripheral IV infusion site, nausea, vomiting, headache
Adefovir	Generally well-tolerated. Nephrotoxicity with underlying renal insufficiency, nausea, asthenia
Albendazole	Nausea, vomiting, hepatotoxicity, hypersensitivity reaction, dizziness, headache, reversible alopecia Rarely: granulocytopenia, agranulocytosis, or pancytopenia
Amikacin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), neuromuscular blockade (associated with rapid infusion of large aminoglycoside doses), pain upon IM injection
Amoxicillin/Clavulate and Ampicillin/Sulbactam	Diarrhea, nausea, vomiting, abdominal pain, <i>Clostridium difficile</i> -associated diarrhea and colitis, hypersensitivity reactions (immediate or delayed reactions including anaphylaxis), bone marrow suppression, drug fever, neurotoxicity at high doses (especially in patients with renal dysfunction)
Amphotericin B Deoxycholate and Lipid Formulations	Nephrotoxicity, infusion-related reactions (fever, chills, rigors, back pain, hypotension), hypokalemia, hypomagnesemia, anemia, thrombophlebitis, nausea, vomiting Liposomal formulations have lower incidence of nephrotoxicity and infusion-related reactions.
Anidulafungin	Generally well-tolerated. Hepatotoxicity, histamine-related infusion reactions (flushing, rash, pruritus, hypotension, dyspnea; rare if infusion rate <1.1 mg/min), hypokalemia, diarrhea
Artemether/Lumefantrine	Generally well-tolerated. Rash, pruritus, nausea, vomiting, abdominal pain, anorexia, diarrhea, arthralgia, myalgia, dizziness, headache, hemolytic anemia (rare), QTc prolongation
Artesunate	Generally well-tolerated. Bradycardia, dizziness, nausea and vomiting, skin rash, pruritus
Atovaquone	Rash, nausea, vomiting, diarrhea, hepatotoxicity, headache, hyperglycemia, fever
Atovaquone/Proguanil	Pruritus, rash, nausea, vomiting, abdominal pain, diarrhea, anorexia, EM, asthenia, dizziness, headache, oral ulcers, hepatotoxicity
Azithromycin	Nausea, vomiting, diarrhea, hepatotoxicity, ototoxicity (with prolonged use), rash, urticaria, pruritus, abdominal pain; risk of torsades de pointes, use with caution in patients with underlying QTc prolongation
Aztreonam	Diarrhea, hypersensitivity reaction (rare), thrombophlebitis
Benznidazole	Photosensitivity, allergic dermatitis, paresthesia, peripheral neuropathy, nausea, vomiting, abdominal pain, anorexia, weight loss
Boceprevir	Anemia, neutropenia, dysgeusia, dry mouth, nausea, headache, acute hypersensitivity reaction (urticarial, angioedema; rare)
Capreomycin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), neuromuscular blockade (associated with rapid infusion of large aminoglycoside doses), pain upon IM injection
Caspofungin	Generally well-tolerated. Fever, thrombophlebitis, histamine-related infusion reactions (flushing, rash, pruritus, facial swelling, hypotension, dyspnea), hypokalemia, anemia, headache, hepatotoxicity
Ceftriaxone	Generally well-tolerated. Cholelithiasis, rash, diarrhea, drug fever, <i>C. difficile</i> -associated diarrhea and colitis; IM injections: injection-site reactions, pain

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 2 of 5)

Drugs	Common or Serious Adverse Reactions
Cephalosporins	Hypersensitivity reaction, rash, nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, bone marrow suppression, CNS toxicities such as seizure and confusion (rare, mostly seen with high dose used in patients with renal insufficiency or elderly patients without dosage adjustment)
Chloroquine and Hydroxychloroquine	Headache, pruritus, skin pigmentation, nausea, vomiting, abdominal pain, diarrhea, anorexia, photosensitivity, visual disturbances, QTc prolongation, neuromyopathy (rarely with long-term use); hemolysis (with G6PD deficiency); hypersensitivity reaction (including TEN, SJS, and EM)
Cidofovir	Nephrotoxicity, proteinuria, ocular hypotony, anterior uveitis/iritis, neutropenia, metabolic acidosis, asthenia. Side effects most likely related to co-administration of probenecid: rash, nausea, vomiting, anorexia
Ciprofloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated age >60 and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or in patients with renal dysfunction), seizures (rare)
Clarithromycin	Hepatotoxicity, ototoxicity (with high doses or prolonged use), headache, nausea, vomiting, abdominal cramps, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, rash, QTc prolongation
Clindamycin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, rash, arrhythmia associated with rapid IV infusion
Clotrimazole (Troche)	Generally well-tolerated. Nausea, vomiting, anorexia, metallic taste, increase in serum transaminases (rare)
Cycloserine	Neuropsychiatric toxicities (headache, somnolence, lethargy, vertigo, tremor, dysarthria, irritability, confusion, paranoia, psychosis), seizures
Dapsone	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), neutropenia, rash, sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, hemolysis), peripheral neuropathy, hepatotoxicity
Doxycycline	Photosensitivity reaction, nausea, vomiting, diarrhea, esophageal ulceration, thrombophlebitis (with IV infusion)
Emtricitabine	Generally well-tolerated. Headache, nausea, hyperpigmentation, diarrhea, rash
Entecavir	Generally well-tolerated. Headache, fatigue, dizziness, nausea
Erythromycin	Nausea, vomiting, abdominal pain, hepatotoxicity, cholestatic jaundice, ototoxicity (hearing loss, tinnitus), rash, QTc prolongation and cardiac arrhythmia
Ethambutol	Optic neuritis (dose dependent), peripheral neuropathy, headache, nausea, vomiting, anorexia, hepatotoxicity, hyperuricemia, hypersensitivity reaction
Ethionamide	Gastrointestinal side effects (dose related): nausea, vomiting, diarrhea, abdominal pain, metallic taste, anorexia; dizziness, drowsiness, depression, hepatotoxicity, hypothyroidism (with or without goiter), gynecomastia
Famciclovir	Generally well-tolerated. Headache, nausea, vomiting, diarrhea
Flucytosine	Concentration-dependent bone marrow suppression (anemia, neutropenia, thrombocytopenia), diarrhea, nausea, vomiting, rash

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 3 of 5)

Drugs	Common or Serious Adverse Reactions
Fluconazole	Hepatotoxicity, rash, nausea, vomiting, diarrhea, abdominal discomfort, reversible alopecia (with doses ≥ 400 mg/d for >2 months)
Foscarnet	Nephrotoxicity, electrolyte imbalances (hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia), penile ulceration, nausea, vomiting, anorexia, headache, seizure (associated with electrolyte imbalances), anemia, injection-site associated thrombophlebitis
Fumagillin (Investigational)	<u>Oral therapy</u> : Neutropenia, thrombocytopenia, vertigo, nausea, vomiting, diarrhea, anorexia, abdominal cramps <u>Ocular therapy</u> : Minimal systemic effect or local effect
Ganciclovir	Neutropenia, thrombocytopenia, anemia, injection-site-associated thrombophlebitis, confusion
Imipenem/Cilastatin	Hypersensitivity reaction (immediate or delayed); CNS effects—seizure, myoclonus, confusion (more frequent with imipenem than meropenem and dorepenem [especially with higher doses, in patients with underlying CNS disorders, or with renal insufficiency]), nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever
Interferon-Alfa and Peginterferon-Alfa	Influenza-like syndrome (fever, headache, fatigue, and myalgia), neuropsychiatric disorders (depression and suicidal ideation), neutropenia, anemia, thrombocytopenia, thyroid dysfunction, injection-site reactions, alopecia, nausea, anorexia, diarrhea, weight loss, development or exacerbation of autoimmune disorders, ocular effects (retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots)
Isoniazid	Hepatotoxicity, peripheral neuropathy, optic neuritis, psychosis (rare)
Itraconazole	Hepatotoxicity, congestive heart failure, edema, hypokalemia, nausea, vomiting, diarrhea, abdominal pain, rash
Lamivudine	Generally well-tolerated. Nausea, vomiting
Levofloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated >60 years of age and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or in patients with renal dysfunction), seizures (rare)
Linezolid	Anemia, neutropenia, thrombocytopenia (especially with >2 - to 4-week treatment), peripheral neuropathy, optic neuritis with long-term (months) therapy, serotonin syndrome (especially in patients receiving concomitant serotonergic agents), seizure (in patients with a history of seizure or with risk factors for seizure), lactic acidosis (rare)
Mefloquine	Depression, psychosis, rash (reports of TEN and SJS), nausea, vomiting, diarrhea, epigastric pain, agitation, dizziness, headache, insomnia, abnormal dreams, QTc prolongation, arrhythmias (extrasystole, sinus bradycardia)
Meropenem	Generally well-tolerated. Hypersensitivity reaction (immediate or delayed), nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever
Micafungin	Generally well-tolerated. Histamine-related infusion reactions (such as flushing, rash, pruritus, hypotension, dyspnea) may occur, but it is rare if infused over 1 hour; anaphylaxis and anaphylactoid reaction; hepatotoxicity, thrombophlebitis, nausea, vomiting, diarrhea, hypokalemia, hemolysis (rare)

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 4 of 5)

Drugs	Common or Serious Adverse Reactions
Miconazole Buccal Tablets	Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, headache, local reactions (oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, pain and swelling, dry mouth), hypersensitivity reaction (rare—may occur in patients with known hypersensitivity reaction to milk product concentrate)
Miltefosine	Nausea, vomiting, diarrhea, leukocytosis, thrombocytosis, nephrotoxicity, retinal degeneration
Moxifloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated >60 years of age and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or in patients with renal dysfunction), seizures (rare)
Nifurtimox	Anorexia, weight loss, nausea, vomiting, abdominal pain, headache, dizziness, mood changes, insomnia, myalgia, peripheral neuropathy, rash, pruritus, memory loss
Nitazoxanide	Generally well-tolerated. Nausea, vomiting, diarrhea, abdominal pain, headache
Nystatin (Oral Preparations)	Unpleasant taste, nausea, vomiting, anorexia, diarrhea, hypersensitivity reaction (rare)
Penicillin G	<u>All Penicillin G Preparations:</u> Hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, drug fever <u>Benzathine Penicillin G & Procaine Penicillin G:</u> IM injection-site reactions (pain and erythema) <u>Aqueous Crystalline Penicillin G (IV):</u> Thrombophlebitis, neurotoxicity at high doses (especially in patients with renal dysfunction)
Pentamidine	<u>IV Infusion:</u> Nephrotoxicity, infusion-related hypotension, thrombophlebitis, arrhythmias (including torsades de pointes), pancreatitis, hypoglycemia, hyperglycemia, diabetes mellitus, hepatotoxicity, electrolyte abnormalities, leukopenia, thrombocytopenia <u>Aerosolized Therapy:</u> Bronchospasm, cough, dyspnea, tachypnea, metallic taste, pancreatitis (rare)
Pentavalent Antimony (Sodium Stibogluconate)	Nausea, vomiting, abdominal pain, anorexia, pancreatitis (rare), headache, hepatotoxicity, arthralgia, myalgia, cardiac toxicity with higher than 20 mg/kg dose, rash, thrombophlebitis, leukopenia, anemia, thrombocytopenia
Posaconazole	Nausea, vomiting, diarrhea, abdominal pain, headache, hepatotoxicity, hypokalemia, QTc prolongation, rash
Piperacillin-Tazobactam	Generally well-tolerated. Hypersensitivity reaction, rash, diarrhea, nausea, vomiting, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, thrombocytopenia (rare), impaired platelet aggregation, seizure (high dose in patients with renal insufficiency)
Primaquine	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), leukopenia, neutropenia, abdominal cramps, nausea, vomiting
Pyrazinamide	Hepatotoxicity, hyperuricemia, arthralgia, nausea, vomiting
Pyrimethamine	Neutropenia, thrombocytopenia, megaloblastic anemia, rash
Quinidine Glucuronate	QTc prolongation, lightheadedness, nausea, vomiting, diarrhea, abdominal pain, drug-induced SLE, headache, rash, hemolysis (with G6PD deficiency), hepatotoxicity
Quinine	Headache, nausea, vomiting, diarrhea, cinchonism (tinnitus, vertigo, blurred vision), hypersensitivity reaction

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 5 of 5)

Drugs	Common or Serious Adverse Reactions
Ribavirin	Hemolytic anemia, dyspnea, hyperbilirubinemia, nausea, vomiting, anorexia, dyspepsia, rash, dry cough
Rifabutin	Hepatotoxicity, uveitis (dose dependent), red-orange discoloration of body fluids, rash, arthralgia, neutropenia, nausea, vomiting, abdominal pain, diarrhea, anorexia
Rifampin	Hepatotoxicity (cholestatic hepatitis), red-orange discoloration of body fluids, thrombocytopenia, hemolytic anemia, rash, hypersensitivity reactions with flu-like syndrome, nausea, vomiting, anorexia, abdominal pain, flatulence, diarrhea, renal failure
Streptomycin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), pain upon IM injection
Sulfadiazine	Rash (including SJS, EM, TEN), anemia, neutropenia, thrombocytopenia, crystalluria with or without urolithiasis, renal insufficiency, nausea, vomiting, drug fever, hepatotoxicity
Telaprevir	Anemia, rash, pruritus, nausea, vomiting, dysgeusia, diarrhea, ano-rectal discomfort (hemorrhoid, pruritus), proctitis, severe cutaneous eruption (including SJS, EM, TEN)
Telbivudine	Generally well-tolerated. Nausea, vomiting, abdominal pain, increase in creatine kinase, headache, dizziness
Tenofovir	Renal insufficiency, proximal renal tubulopathy (with hypophosphatemia, hypouricemia, normoglycemic glycosuria), decrease in bone mineral density, nausea
Tetracycline	Photosensitivity, tooth discoloration if taken by infants and children, pruritus, esophageal ulceration, nausea, vomiting, diarrhea, hepatotoxicity, rash
Trimethoprim-Sulfamethoxazole	Rash (including SJS, EM, and TEN), photosensitivity, anemia, neutropenia, thrombocytopenia, hepatotoxicity, increase in serum creatinine (without change in GFR), interstitial nephritis, nausea, vomiting, crystalluria (in patients with inadequate hydration), hyperkalemia (more common with high dose TMP), drug fever
Valacyclovir	Generally well-tolerated. Nausea, vomiting, headache, crystalluria (with high dose or renal impairment), neurotoxicity (high doses, especially in patients with renal impairment; agitation, confusion, hallucination, seizure, coma)
Valganciclovir	Neutropenia, thrombocytopenia, anemia, nausea, vomiting, diarrhea, confusion
Vancomycin	Infusion-related reaction (infusion-rate related, flushing, hypotension, rash), thrombophlebitis, rash, neutropenia, thrombocytopenia (rare), ototoxicity (associated with excessive concentration), nephrotoxicity (associated with high daily dose and high trough concentrations)
Voriconazole	Visual disturbances (with initial dosing), optic neuritis (with >28 days treatment), skin photosensitivity, rash, hepatotoxicity, peripheral edema, headache, delirium, hallucination, encephalopathy (associated with trough >5.5 mcg/mL), QTc prolongation, peripheral neuropathy (rare)

Key to Acronyms: CNS = central nervous system; EM = erythema multiforme; G6PD = glucose-6-phosphate dehydrogenase; GFR = glomerular filtration rate; IM = intramuscular; IV = intravenous; SJS = Stevens-Johnson syndrome; SLE = systemic lupus erythematosus; TEN = toxic epidermal necrolysis; TMP = trimethoprim

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 1 of 7)
(Last updated May 7, 2013; last reviewed May 7, 2013)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Acyclovir	IV dose for: • serious HSV - 5 mg/kg IV q8h, <i>or</i> • VZV infections - 10 mg/kg IV q8h	25–50	100% of dose IV q12h
		10–25	100% of dose IV q24h
		<10	50% of dose IV q24h
		hemodialysis	50% of dose q24h; administer after dialysis on day of dialysis
	PO Dose for Herpes Zoster: 800 mg PO 5 times/day	10–25	800 mg PO q8h
		<10	800 mg PO q12h
		hemodialysis	800 mg PO q12h; administer dose after dialysis
Adefovir	10 mg PO q24h	30–49	10 mg PO q48h
		10–29	10 mg PO q72h
		hemodialysis	10 mg PO weekly (dose after dialysis)
Amikacin (for mycobacterial infections)	IV 15 mg/kg/day or 25 mg/kg TIW	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations with target peak concentration 35–45 mcg/mL and trough concentration <4 mcg/mL.
Amphotericin B	• 0.7–1.0 mg/kg/day IV (amphotericin B deoxycholate), <i>or</i> • 3–6 mg/kg/day IV (lipid formulation)		No dosage adjustment necessary; alternative antifungals should be considered if renal insufficiency occurs during therapy despite adequate hydration.
Capreomycin	15 mg/kg (maximum dose 1000 mg) IV or IM per day	Use with caution in patients with renal insufficiency.	Refer to product label for dosing guidelines based on creatinine clearance. Consider monitoring capreomycin serum concentrations.
Chloroquine (base)	For Treatment of Acute Malaria: • 600 mg PO for 1 dose, followed by 300 mg PO at 6, 24, and 48 hours (for a total dose of 1500 mg)	<10	50% of dose
Cidofovir	• 5 mg/kg IV on days 0, repeat 5 mg/kg IV dose at day 7, then 5 mg/kg IV every 2 weeks (days 21, 35, 49, 63, etc.) Each dose should be given with probenecid and saline hydration (see Table 2).	• Pretreatment SCr >1.5 mg/dL, <i>or</i> • CrCl < 55 mL/min, <i>or</i> • >100 mg/dL (>2+) protein in urinalysis	Cidofovir is not recommended
		If SCr increases by 0.3–0.4 mg/dL from baseline	3 mg/kg IV per dose
		• If SCr increases >0.5 mg/dL >baseline, <i>or</i> • ≥3+ proteinuria	Discontinue therapy

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 2 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Ciprofloxacin	<ul style="list-style-type: none"> • 500–750 mg PO q12h, <i>or</i> • 400 mg IV q8–12h 	<30	250–500 mg PO q24h <i>or</i> 400 mg IV q24h
		hemodialysis or peritoneal dialysis	250–500 mg PO q24hr <i>or</i> 200–400 mg IV q24h (administered after dialysis)
Clarithromycin	500 mg PO BID	<30	250 mg PO BID or 500 mg PO once daily
Cycloserine	10 mg/kg/day PO in 2 divided doses (maximum 1000 mg/day)	50–80	Normal dose, consider monitoring serum concentration and toxicities
		<50 (not on hemodialysis)	Not recommended because of accumulation and toxicities.
		hemodialysis	250 mg PO once daily or 500 mg PO TIW—consider monitoring serum cycloserine concentration
Emtricitabine	<ul style="list-style-type: none"> • 200-mg tablet PO once daily, <i>or</i> • 240-mg solution PO once daily 		<u>Oral Tablets</u> <u>Oral Solution</u>
		30–49	200 mg q48h 120 mg q24h
		15–29	200 mg q72h 80 mg q24h
		<15 or hemodialysis (dose after dialysis)	200 mg q96h 60 mg q24h
Emtricitabine/Tenofovir (co-formulation as Truvada) Please refer to product information for dosing recommendations for other ARV fixed dose combination product containing tenofovir/emtricitabine.	200 mg/300 mg - 1 tablet PO daily	30–49	1 tablet PO q48h (monitor for worsening renal function; consider alternative to TDF)
		<30 or hemodialysis	Co-formulated tablet should not be used for CrCl <30 mL/min. Use individual formulation and adjust dose according to recommendations for individual drugs.

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 3 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Entecavir	Usual Dose: • 0.5 mg PO once daily For Treatment of 3TC-Refractory HBV or for Patients with Decompensated Liver Disease: • 1 mg PO once daily		Usual Dose	3TC-Refractory or Decompensated Liver Disease
		30 to <50	• 0.25 mg q24h, <i>or</i> • 0.5 mg q48h	• 0.5 mg q24h, <i>or</i> • 1 mg q48h
		10 to <30	• 0.15 mg q24h, <i>or</i> • 0.5 mg q72h	• 0.3 mg q24h, <i>or</i> • 1 mg q72h
		<10 or hemodialysis or CAPD (administer after dialysis on dialysis day)	• 0.05 mg q24h, <i>or</i> • 0.5 mg q7 days	• 0.1 mg q24h, <i>or</i> • 1 mg q7 days
Ethambutol	• 15–25 mg/kg PO daily • (15 mg/kg PO daily for MAI; 15–25 mg/kg PO daily for MTB)	10–50	15–25 mg/kg q24–36h	
		<10	15–25 mg/kg q48h	
		hemodialysis	15–25 mg/kg TIW after hemodialysis Can consider TDM to guide optimal dosing	
Famciclovir	For Herpes Zoster: • 500 mg PO q8h	40–59	500 mg PO q12h	
		20–39	500 mg PO q24h	
		<20	250 mg PO q24h	
		hemodialysis	250 mg PO after each dialysis	
Fluconazole	200–1200 mg PO or IV q24h	≤50	50% of dose q24h	
		hemodialysis	Full dose after each dialysis	
Flucytosine	25 mg/kg PO q6h If available, TDM is recommended for all patients to guide optimal dosing (goal peak 30–80 mcg/mL 2 hour post dose)	20–40	25 mg/kg q12h	
		10–20	25 mg/kg q24h	
		<10	25 mg/kg q48h	
		hemodialysis	25–50 mg/kg q48–72h (after hemodialysis)	
Foscarnet	180 mg/kg/day IV in 2 divided doses for induction therapy for CMV infection 90–120 mg/kg IV once daily for maintenance therapy for CMV infection or for treatment of HSV infections	Dosage adjustment needed according to calculated CrCl/kg; consult product label for dosing table.		

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 4 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Ganciclovir	<u>Induction Therapy:</u> • 5 mg/kg IV q12h	50–69	2.5 mg/kg IV q12h	
		25–49	2.5 mg/kg IV q24h	
		10–24	1.25 mg/kg IV q24h	
		<10 or on hemodialysis	1.25 mg/kg IV TIW after dialysis	
	<u>Maintenance Therapy:</u> • 5 mg/kg IV q24h	50–69	2.5 mg/kg IV q24h	
		25–49	1.25 mg/kg IV q24h	
		10–24	0.625 mg/kg IV q24h	
		<10 or on hemodialysis	0.625 mg/kg IV TIW after dialysis	
Lamivudine	300 mg PO q24h	30–49	150 mg PO q24h	
		15–29	150 mg PO once, then 100 mg PO q24h	
		5–14	150 mg PO once, then 50 mg PO q24h	
		<5 or on hemodialysis	50 mg PO once, then 25 mg PO q24h (give the dose after dialysis on dialysis day)	
Levofloxacin	500 mg (low dose) or 750 mg (high dose) IV or PO daily <u>Nosocomial Pneumonia/ Osteomyelitis:</u> • 750 mg daily	20–49	<u>Lower Dose</u> 500 mg once, then 250 mg q24h	<u>High Dose</u> 750 mg q48h
		<19 or on CAPD or hemodialysis (dose after dialysis)	500 mg once, then 250 mg q48h	750 mg once, then 500 mg q48h
Peginterferon Alfa-2a	180 mcg SQ once weekly	<30 hemodialysis	135 mcg SQ once weekly	
Peginterferon Alfa-2b	1.5 mcg/kg SQ once weekly	30–50	Reduce dose by 25%	
		10–29 and hemodialysis	Reduce dose by 50%	
Penicillin G Potassium (or sodium)	<u>Neurosyphilis or Ocular/Otic Syphilis:</u> • 3–4 million units IV q4h, <i>or</i> • 18–24 million units IV daily as continuous infusion	10–50	2–3 million units q4h or 12–18 million units as continuous infusion	
		<10	2 million units q4–6h or 8–12 million units as continuous infusion	
		hemodialysis or CAPD	2 million units q6h or 8 million units as continuous infusion	
Pentamidine	4 mg/kg IV q24h	10–50	3 mg/kg IV q24h	
		<10	4 mg/kg IV q48h	

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 5 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Pyrazinamide	See Table 3 for weight-based dosing guidelines	<10	50% of usual dose
		hemodialysis	Usual dose given after dialysis
Quinidine Gluconate (salt) (10 mg quinidine gluconate salt = 6.25 mg quinidine base)	<u>Loading Dose:</u> • 10 mg/kg (salt) IV over 1–2 hours, then 0.02 mg/kg/min (salt) IV for up to 72 hours or until able to take PO meds Consider TDM for all patients to optimize dosing.	<10	75% of normal dose
		hemodialysis	75% of normal dose; some clinicians recommend supplementation with 100 mg–200 mg after dialysis.
Quinine Sulfate	650 mg salt (524 mg base) PO q8h	<10 or hemodialysis	650 mg once, then 325 mg PO q12h
Ribavirin	For genotypes 1 and 4: • 1000–1200 mg PO per day in 2 divided doses (based on weight, see Table 2 for full dosing recommendation) For genotype 2 and 3: • 400 mg PO BID for genotypes 2 and 3	30–50	Alternate dosing 200 mg PO and 400 mg PO every other day
		<30 or hemodialysis	200 mg PO daily
Rifabutin	300 mg PO daily (see Table 5 for dosage adjustment based on drug-drug interaction)	<30	50% of dose once daily. Consider TDM
Streptomycin	• 15 mg/kg IM or IV q24h, <i>or</i> • 25 mg/kg IM or IV TIW	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations.
Sulfadiazine	1000–1500 mg PO q6h (1500 mg q6h for >60kg)	10–50	1000–1500 mg PO q12h (ensure adequate hydration)
		<10 or hemodialysis	1000–1500 mg PO q24h (dose after HD on days of dialysis)
Telbivudine	600 mg PO daily	30–49	Oral tablets: 600 mg PO q48h Oral solution: 400 mg PO q24h
		<30	Oral tablets: 600 mg PO q72h Oral solution: 200 mg PO q24h
		hemodialysis	Oral tablets: 600 mg PO q96h (dose after dialysis) Oral solution: 120 mg PO q24h (dose after dialysis on dialysis day)

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 6 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Tenofovir	300 mg PO daily	30–49	300 mg PO q48h	
		10–29	300 mg PO q72–96h	
		<10 and not on dialysis	Not recommended	
		hemodialysis	300 mg PO once weekly (dose after dialysis) Can consider alternative agent for treatment of HBV and/or HIV if TDF-associated renal toxicity occurs.	
Tetracycline	250 mg PO q6h Consider using doxycycline in patients with renal dysfunction.	10–49	250 mg PO q12–24h	
		<10	250 mg PO q24h	
		hemodialysis	250 mg PO q24h; dose after dialysis	
Trimethoprim/ Sulfamethoxazole	For PCP Treatment: • 5 mg/kg (of TMP component) IV q8h, <i>or</i> • 2 DS tablets PO q8h	10–30	5 mg/kg (TMP) IV q12h or TMP-SMX 2 DS tablets PO q12h	
		<10	5 mg/kg (TMP) IV q24h, or TMP-SMX DS tablet PO q12h (or 2 TMP-SMX DS tablets q24h)	
		hemodialysis	5 mg/kg/day (TMP) IV or 2 TMP-SMX DS tablets PO; dose after dialysis on dialysis day Can consider TDM to optimize therapy (target TMP concentrations: 5–8 mcg/mL)	
Valacyclovir	For Herpes Zoster: • 1 g PO TID	30–49	1 g PO q12h	
		10–29	1 g PO q24h	
		<10	500 mg PO q24h	
		hemodialysis	500 mg PO q24h; dose after dialysis on dialysis days	
Valganciclovir	Induction Therapy: • 900 mg PO BID Maintenance Therapy: • 900 mg PO daily	40–59	Induction 450 mg PO BID	Maintenance 450 mg PO daily
		25–39	450 mg PO daily	450 mg PO q48h
		10–25	450 mg PO q48h	450 mg PO BIW
		<10 not on dialysis	not recommended	not recommended
		hemodialysis (clinical efficacy of this dosage has not been established)	200 mg PO TIW after dialysis (oral powder formulation)	100 mg PO TIW after dialysis (oral powder formulation)

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 7 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Voriconazole	<ul style="list-style-type: none"> • 6 mg/kg IV q12h 2 times, then 4 mg/kg q12h, <i>or</i> • 200–300 mg PO q12h 	<50	<p>IV voriconazole is not recommended because of potential toxicity due to accumulation of sulfobutylether cyclodextrin (vehicle of IV product).</p> <p>Should switch to PO voriconazole in these patients. No need for dosage adjustment when PO dose is used.</p>

Key to Acronyms: 3TC = lamivudine; BID = twice daily; BIW = twice weekly; CAPD = continuous ambulatory peritoneal dialysis; CMV = cytomegalovirus; CrCl = creatinine clearance; DS = double strength; HBV = hepatitis B virus; HSV = herpes simplex virus; IM = intramuscular; IV = intravenous; MAI = *Mycobacterium avium intracellulare*; MTB = *Mycobacterium tuberculosis*; PCP = *Pneumocystis pneumonia*; PO = orally; q(n)h = every “n” hours; SQ = subcutaneous; SCr = ; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TID = three times daily; TIW = three times weekly; TMP = trimethoprim; SMX = sulfamethoxazole; VZV = varicella zoster virus

Creatinine Clearance Calculation	
<p>Male:</p> $\frac{(140 - \text{age in years}) \times \text{weight (kg)}}{72 \times \text{Serum Creatinine}}$	<p>Female:</p> $\frac{(140 - \text{age in years}) \times \text{weight (kg)} \times 0.85}{72 \times \text{Serum Creatinine}}$

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 1 of 9) (Last updated May 7, 2013; last reviewed May 7, 2013)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Acyclovir	B	No teratogenicity in mice, rats, rabbits at human levels. Large experience in pregnancy (>700 first-trimester exposures reported to registry); well-tolerated.	Treatment of frequent or severe symptomatic herpes outbreaks or varicella
Adefovir	C	No increase in malformations at 23 times (rats) and 40 times (rabbits) human dose. Limited experience with human use in pregnancy.	Not recommended because of limited data in pregnancy. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com
Albendazole	C	Embryotoxic and teratogenic (skeletal malformations) in rats and rabbits, but not in mice or cows. Limited experience in human pregnancy.	Not recommended, especially in first trimester. Primary therapy for microsporidiosis in pregnancy should be ART.
Amikacin	C	Not teratogenic in mice, rats, rabbits. Theoretical risk of ototoxicity in fetus; reported with streptomycin but not amikacin.	Drug-resistant TB, severe MAC infections
Amoxicillin, amox./clavulanate, ampicillin/sulbactam	B	Not teratogenic in animals. Large experience in human pregnancy does not suggest an increase in adverse events.	Susceptible bacterial infections
Amphotericin B	B	Not teratogenic in animals or in human experience. Preferred over azole antifungals in first trimester if similar efficacy expected.	Documented invasive fungal disease
Antimonials, pentavalent (stibogluconate, meglumine)	Not FDA approved	Antimony not teratogenic in rats, chicks, sheep. Three cases reported of use in human pregnancy in second trimester with good outcome. Labeled as contraindicated in pregnancy.	Therapy of visceral leishmaniasis not responsive to amphotericin B or pentamidine
Artesunate, artemether, artemether/lumefantrine	C	Embryotoxicity, cardiovascular and skeletal anomalies in rats and rabbits. Embryotoxic in monkeys. Human experience, primarily in the second and third trimesters, has not identified increased adverse events.	Recommended by WHO as first-line therapy in second/third trimester for <i>P. falciparum</i> and severe malaria. Pending more data, use for malaria in first trimester only if other drugs not available or have failed. Report cases of exposure to WHO Anti-malarial Pregnancy Exposure Registry when available.
Atovaquone	C	Not teratogenic in rats or rabbits, limited human experience	Alternate agent for PCP, <i>Toxoplasma gondii</i> , malaria infections
Azithromycin	B	Not teratogenic in animals. Moderate experience with use in human pregnancy does not suggest adverse events.	Preferred agent for MAC prophylaxis or treatment (with ethambutol), <i>Chlamydia trachomatis</i> infection in pregnancy.
Aztreonam	B	Not teratogenic in rats, rabbits. Limited human experience, but other beta-lactam antibiotics have not been associated with adverse pregnancy outcomes.	Susceptible bacterial infections
Benznidazole	Not FDA approved	No animal studies. Increase in chromosomal aberrations in children with treatment; uncertain significance. No human pregnancy data.	Not indicated for chronic <i>T. cruzi</i> in pregnancy. Seek expert consultation if acute or symptomatic infection in pregnancy requiring treatment.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 2 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Boceprevir	B	Not teratogenic in rats, rabbits. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy.
Capreomycin	C	Increase in skeletal variants in rats. Limited experience in human pregnancy; theoretical risk of fetal ototoxicity.	Drug-resistant TB
Caspofungin	C	Embryotoxic, skeletal defects in rats, rabbits. No experience with human use.	Invasive <i>Candida</i> or <i>Aspergillus</i> infections refractory to amphotericin and azoles
Cephalosporins	B	Not teratogenic in animals. Large experience in human pregnancy has not suggested increase in adverse outcomes.	Bacterial infections; alternate treatment for MAC
Chloroquine	C	Associated with anophthalmia, microphthalmia at fetotoxic doses in animals. Not associated with increased risk in human pregnancy at doses used for malaria.	Drug of choice for malaria prophylaxis and treatment of sensitive species in pregnancy.
Cidofovir	C	Embryotoxic and teratogenic (meningocoele, skeletal abnormalities) in rats and rabbits. No experience in human pregnancy.	Not recommended
Ciprofloxacin, other quinolones	C	Arthropathy in immature animals; not embryotoxic or teratogenic in mice, rats, rabbits, or monkeys. More than 1100 cases of quinolone use in human pregnancy have not been associated with arthropathy or birth defects.	Severe MAC infections; multidrug resistant TB, anthrax, bacterial infections
Clarithromycin	C	Cardiovascular defects noted in one strain of rats and cleft palate in mice at high doses, not teratogenic in rabbits or monkeys. Two human studies, each with >100 first-trimester exposures, did not show increase in defects but one study found an increase in spontaneous abortion.	Treatment or secondary MAC prophylaxis, if other choices exhausted
Clindamycin	B	No concerns specific to pregnancy in animal or human studies.	Treatment of anaerobic bacterial infections and used with quinine for chloroquine-resistant malaria; alternate agent for secondary prophylaxis of <i>Toxoplasma</i> encephalitis
Clofazimine	C	Not teratogenic in mice, rats, or rabbits. Limited experience reported (19 cases); no anomalies noted but red-brown skin discoloration reported in several infants exposed throughout pregnancy.	No indications.
Clotrimazole troches	C	Not teratogenic in animals at exposures expected from treatment of oral or vaginal <i>Candida</i> . No increase in adverse pregnancy outcomes with vaginal use.	Oral or vaginal <i>Candida</i> infections and prophylaxis
Cycloserine	C	Not teratogenic in rats. No data available from human studies.	Drug-resistant TB

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 3 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Dapsone	C	No animal data. Limited human experience does not suggest teratogenicity; might displace bound bilirubin in the neonate, increasing the risk of kernicterus. Case reports of hemolytic anemia in fetus/infant with maternal treatment.	Alternate choice for primary or secondary PCP prophylaxis
Diphenoxylate	C	Limited animal and human data do not indicate teratogenicity.	Symptomatic treatment of diarrhea
Doxycycline, other tetracyclines	D	Risk of hepatic toxicity increased with tetracyclines in pregnancy; staining of fetal bones and teeth contraindicates use in pregnancy.	No indications
Emtricitabine	B	No concerns in pregnancy from limited animal and human data.	As part of fully suppressive combination antiretroviral regimen for treatment of HIV, HBV. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Entecavir	C	Animal data do not suggest teratogenicity at human doses; limited experience in human pregnancy.	Not recommended because of limited data in pregnancy. Use as part of fully suppressive ARV regimen with ARV agents active against both HIV and HBV. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Erythromycin	B	Hepatotoxicity with erythromycin estolate in pregnancy; other forms acceptable; no evidence of teratogenicity	Bacterial and chlamydial infections
Ethambutol	B	Teratogenic, at high doses, in mice, rats, rabbits. No evidence of teratogenicity in 320 cases of human use for treatment of TB.	Active TB and MAC treatment; avoid in first trimester if possible
Ethionamide	C	Increased rate of defects (omphalocele, exencephaly, cleft palate) in rats, mice, and rabbits with high doses; not seen with usual human doses. Limited human data; case reports of CNS defects.	Active TB; avoid in first trimester if possible
Famciclovir	B	No evidence of teratogenicity in rats or rabbits, limited human experience.	Recurrent genital herpes and primary varicella infection. Report exposures during pregnancy to the Famvir Pregnancy Registry (1-888-669-6682).
Fluconazole	C	Abnormal ossification, structural defects in rats, mice at high doses. Case reports of rare pattern of craniofacial, skeletal and other abnormalities in five infants born to four women with prolonged exposure during pregnancy; no increase in defects seen in several series after single dose treatment.	Single dose may be used for treatment of vaginal <i>Candida</i> though topical therapy preferred. Not recommended for prophylaxis during early pregnancy. Can be used for invasive fungal infections after first trimester; amphotericin B preferred in first trimester if similar efficacy expected.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 4 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Flucytosine	C	Facial clefts and skeletal defects in rats; cleft palate in mice, no defects in rabbits. No reports of use in first trimester of human pregnancy; may be metabolized to 5-fluorouracil, which is teratogenic in animals and possibly in humans.	Use after first trimester if indicated for life-threatening fungal infections.
Foscarnet	C	Skeletal variants in rats, rabbits and hypoplastic dental enamel in rats. Single case report of use in human pregnancy in third trimester.	Alternate agent for treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection.
Fumagillin	Not FDA approved	Caused complete litter destruction or growth retardation in rats, depending on when administered. No data in human pregnancy.	Topical solution can be used for ocular microsporidial infections.
Ganciclovir, valganciclovir	C	Embryotoxic in rabbits and mice; teratogenic in rabbits (cleft palate, anophthalmia, aplastic kidney and pancreas, hydrocephalus). Case reports of safe use in human pregnancy after transplants, treatment of fetal CMV.	Treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection. Preferred agent for therapy in children.
Imipenem, meropenem	C/B	Not teratogenic in animals; limited human experience.	Serious bacterial infections
Imiquimod	B	Not teratogenic in rats and rabbits; 8 case reports of human use, only 2 in first trimester.	Because of limited experience, other treatment modalities such as cryotherapy or trichloroacetic acid recommended for wart treatment during pregnancy.
Influenza vaccine	C	Not teratogenic. Live vaccines, including intranasal influenza vaccine, are contraindicated in pregnancy.	All pregnant women should receive injectable influenza vaccine because of the increased risk of complications of influenza during pregnancy. Ideally, HIV-infected women should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Interferons (alfa, beta, gamma)	C	Abortifacient at high doses in monkeys, mice; not teratogenic in monkeys, mice, rats, or rabbits. Approximately 30 cases of use of interferon-alfa in pregnancy reported; 14 in first trimester without increase in anomalies; possible increased risk of intrauterine growth retardation.	Not indicated. Treatment of HCV currently generally not recommended in pregnancy.
Isoniazid	C	Not teratogenic in animals. Possible increased risk of hepatotoxicity during pregnancy; prophylactic pyridoxine, 50 mg/day, should be given to prevent maternal and fetal neurotoxicity.	Active TB; prophylaxis for exposure or skin test conversion

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 5 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Itraconazole	C	Teratogenic in rats and mice at high doses. Case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy; no increase in defect rate noted among over 300 infants born after first-trimester itraconazole exposure.	Only for documented systemic fungal disease, not prophylaxis. Consider using amphotericin B in first trimester if similar efficacy expected.
Kanamycin	D	Associated with club feet in mice, inner ear changes in multiple species. Hearing loss in 2.3% of 391 children after long-term <i>in utero</i> therapy.	Drug-resistant TB
Ketoconazole	C	Teratogenic in rats, increased fetal death in mice, rabbits. Inhibits androgen and corticosteroid synthesis; may impact fetal male genital development; case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy.	None
Lamivudine	C	Not teratogenic in animals. No evidence of teratogenicity with >3700 first-trimester exposures reported to Antiretroviral Pregnancy Registry.	HIV and HBV therapy, only as part of a fully suppressive combination ARV regimen. Report exposures to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Leucovorin (folinic acid)	C	Prevents birth defects of valproic acid, methotrexate, phenytoin, aminopterin in animal models. No evidence of harm in human pregnancies.	Use with pyrimethamine if use of pyrimethamine cannot be avoided.
Linezolid	C	Not teratogenic in animals. Decreased fetal weight and neonatal survival at ~ human exposures, possibly related to maternal toxicity. Limited human experience.	Serious bacterial infections
Loperamide	B	Not teratogenic in animals. No increase in birth defects among infants born to 89 women with first-trimester exposure in one study; another study suggests a possible increased risk of hypospadias with first-trimester exposure, but confirmation required.	Symptomatic treatment of diarrhea after the first trimester
Mefloquine	C	Animal data and human data do not suggest an increased risk of birth defects, but miscarriage and stillbirth may be increased.	Second-line therapy of chloroquine-resistant malaria in pregnancy, if quinine/clindamycin not available or not tolerated. Weekly as prophylaxis in areas with chloroquine-resistant malaria.
Meglumine	Not FDA approved	See Antimonials, pentavalent	
Metronidazole	B	Multiple studies do not indicate teratogenicity. Studies on several hundred women with first-trimester exposure found no increase in birth defects.	Anaerobic bacterial infections, bacterial vaginosis, trichomoniasis, giardiasis, amebiasis

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 6 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Micafungin	C	Teratogenic in rabbits; no human experience.	Not recommended
Miltefosine	Not FDA approved	Embryotoxic in rats, rabbits; teratogenic in rats. No experience with human use.	Not recommended
Nifurtimox	Not FDA approved	Not teratogenic in mice and rats. Increased chromosomal aberrations in children receiving treatment; uncertain significance. No experience in human pregnancy.	Not indicated in chronic infection; seek expert consultation if acute infection or symptomatic reactivation of <i>T. cruzi</i> in pregnancy.
Nitazoxanide	B	Not teratogenic in animals; no human data	Severely symptomatic cryptosporidiosis after the first trimester
Para-amino salicylic acid (PAS)	C	Occipital bone defects in one study in rats; not teratogenic in rabbits. Possible increase in limb, ear anomalies in one study with 143 first-trimester exposures; no specific pattern of defects noted, several studies did not find increased risk.	Drug-resistant TB
Paromomycin	C	Not teratogenic in mice and rabbits. Limited human experience, but poor oral absorption makes toxicity, teratogenicity unlikely.	Amebic intestinal infections, possibly cryptosporidiosis
Penicillin	B	Not teratogenic in multiple animal species. Vast experience with use in human pregnancy does not suggest teratogenicity, other adverse outcomes.	Syphilis, other susceptible bacterial infections
Pentamidine	C	Embryocidal but not teratogenic in rats, rabbits with systemic use. Limited experience with systemic use in pregnancy.	Alternate therapy for PCP and leishmaniasis.
Piperacillin-tazobactam	B	Not teratogenic in limited animal studies. Limited experience in pregnancy but penicillins generally considered safe.	Bacterial infections
Pneumococcal vaccine	C	No studies in animal pregnancy. Polysaccharide vaccines generally considered safe in pregnancy. Well-tolerated in third-trimester studies.	Initial or booster dose for prevention of invasive pneumococcal infections. HIV-infected pregnant women should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Podophyllin, podofilox	C	Increased embryonic and fetal deaths in rats, mice but not teratogenic. Case reports of maternal, fetal deaths after use of podophyllin resin in pregnancy; no clear increase in birth defects with first-trimester exposure.	Because alternative treatments for genital warts in pregnancy are available, use not recommended; inadvertent use in early pregnancy is not indication for abortion.
Posaconazole	C	Embryotoxic in rabbits; teratogenic in rats at similar to human exposures. No experience in human pregnancy.	Not recommended

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 7 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Prednisone	B	Dose-dependent increased risk of cleft palate in mice, rabbits, hamsters; dose-dependent increase in genital anomalies in mice. Human data inconsistent regarding increased risk of cleft palate. Risk of growth retardation, low birth weight may be increased with chronic use; monitor for hyperglycemia with use in third trimester.	Adjunctive therapy for severe PCP; multiple other non-HIV-related indications
Primaquine	C	No animal data. Limited experience with use in human pregnancy; theoretical risk for hemolytic anemia if fetus has G6PD deficiency.	Alternate therapy for PCP, chloroquine-resistant malaria
Proguanil	C	Not teratogenic in animals. Widely used in malaria-endemic areas with no clear increase in adverse outcomes.	Alternate therapy and prophylaxis of <i>P. falciparum</i> malaria
Pyrazinamide	C	Not teratogenic in rats, mice. Limited experience with use in human pregnancy.	Active TB
Pyrimethamine	C	Teratogenic in mice, rats, hamsters (cleft palate, neural tube defects, and limb anomalies). Limited human data have not suggested an increased risk of birth defects; because folate antagonist, use with leucovorin.	Treatment and secondary prophylaxis of toxoplasmic encephalitis; alternate treatment of PCP
Quinidine gluconate	C	Generally considered safe in pregnancy; high doses associated with preterm labor. One case of fetal 8th nerve damage reported.	Alternate treatment of malaria, control of fetal arrhythmias
Quinine sulfate	C	High doses, often taken as an abortifacient, have been associated with birth defects, especially deafness, in humans and animals. Therapeutic doses have not been associated with an increased risk of defects in humans or animals. Monitor for hypoglycemia.	Treatment of chloroquine-resistant malaria
Ribavirin	X	Dose-dependent risk of multiple defects (craniofacial, central nervous system, skeletal, anophthalmia) in rats, mice, hamsters starting at below human doses. Reports of treatment during second half of pregnancy in nine women without incident; first 49 cases in registry did not suggest increased risk, but limited data.	Contraindicated in early pregnancy; no clear indications in pregnancy. Report exposures during pregnancy to Ribavirin Pregnancy Registry at (800) 593-2214 or www.ribavirinpregnancyregistry.com
Rifabutin	B	Not teratogenic in rats and rabbits; no specific concerns for human pregnancy.	Treatment or prophylaxis of MAC, active TB
Rifampin	C	Teratogenic at high doses in mice (cleft palate) and rats (spina bifida) but not in rabbits. No clear teratogenicity in humans.	Active TB
Streptomycin	D	No teratogenicity in mice, rats, guinea pigs. Possible increased risk of deafness and VIII nerve damage; no evidence of other defects.	Alternate therapy for active TB

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 8 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Sulfadiazine	B	Sulfonamides teratogenic in some animal studies. No clear teratogenicity in humans; potential for increased jaundice, kernicterus if used near delivery.	Secondary prophylaxis of toxoplasmic encephalitis
Telaprevir	B	Not teratogenic in mice, rats. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy.
Telbivudine	B	Not teratogenic in rats, rabbits. Limited experience in human pregnancy.	Not recommended because of limited data in pregnancy. Use as part of fully suppressive antiretroviral regimen with antiretroviral agents active against both HIV and hepatitis B. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Tenofovir	B	No evidence of birth defects in rats, rabbits, or monkeys at high doses; chronic administration in immature animals of multiple species at 6–50 times human doses has led to dose-specific bone changes ranging from decreased mineral density to severe osteomalacia and fractures. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown. No evidence of increased birth defects in nearly 2000 first-trimester exposures in women.	Component of fully suppressive antiretroviral regimen in pregnant women. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Trichloroacetic acid, bichloroacetic acid	Not rated	No studies. Used topically so no systemic absorption expected.	Topical therapy of non-cervical genital warts
Trifluridine	C	Not teratogenic in rats, rabbits. Minimal systemic absorption expected with topical ocular use.	Topical agent for treatment of ocular herpes infections
Trimethoprim-sulfamethoxazole	C	Teratogenic in rats and mice. Possible increase in congenital cardiac defects, facial clefts, neural tube and urinary defects with first-trimester use. Unclear if higher levels of folate supplementation lower risk. Theoretical risk of elevated bilirubin in the neonate if used near delivery.	Therapy of PCP during pregnancy. Primary and secondary PCP prophylaxis in the second/third trimester; consider aerosolized pentamidine in first trimester. Recommend fetal ultrasound at 18–20 weeks after first-trimester exposure.
Valacyclovir	B	Not teratogenic in mice, rats, and rabbits. Experience with valacyclovir in pregnancy limited; prodrug of acyclovir, which is considered safe for use in pregnancy.	Treatment of HSV and varicella infections in pregnancy
Vancomycin	C	Not teratogenic in rats, rabbits. Limited human experience.	Serious bacterial infections

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 9 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Voriconazole	D	Embryotoxic in rats, rabbits. Teratogenic in rats (cleft palate, hydronephrosis, and ossification defects). No experience with human use.	Not recommended

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; CMV = cytomegalovirus; CNS = central nervous system; FDA = Food and Drug Administration; G6PD = Glucose-6-phosphate dehydrogenase; HBV = hepatitis B virus; HCV = hepatitis C virus; HSV = herpes simplex virus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; TB = tuberculosis; VIII nerve = vestibulocochlear nerve; WHO = World Health Organization